Tuberculosis

BY

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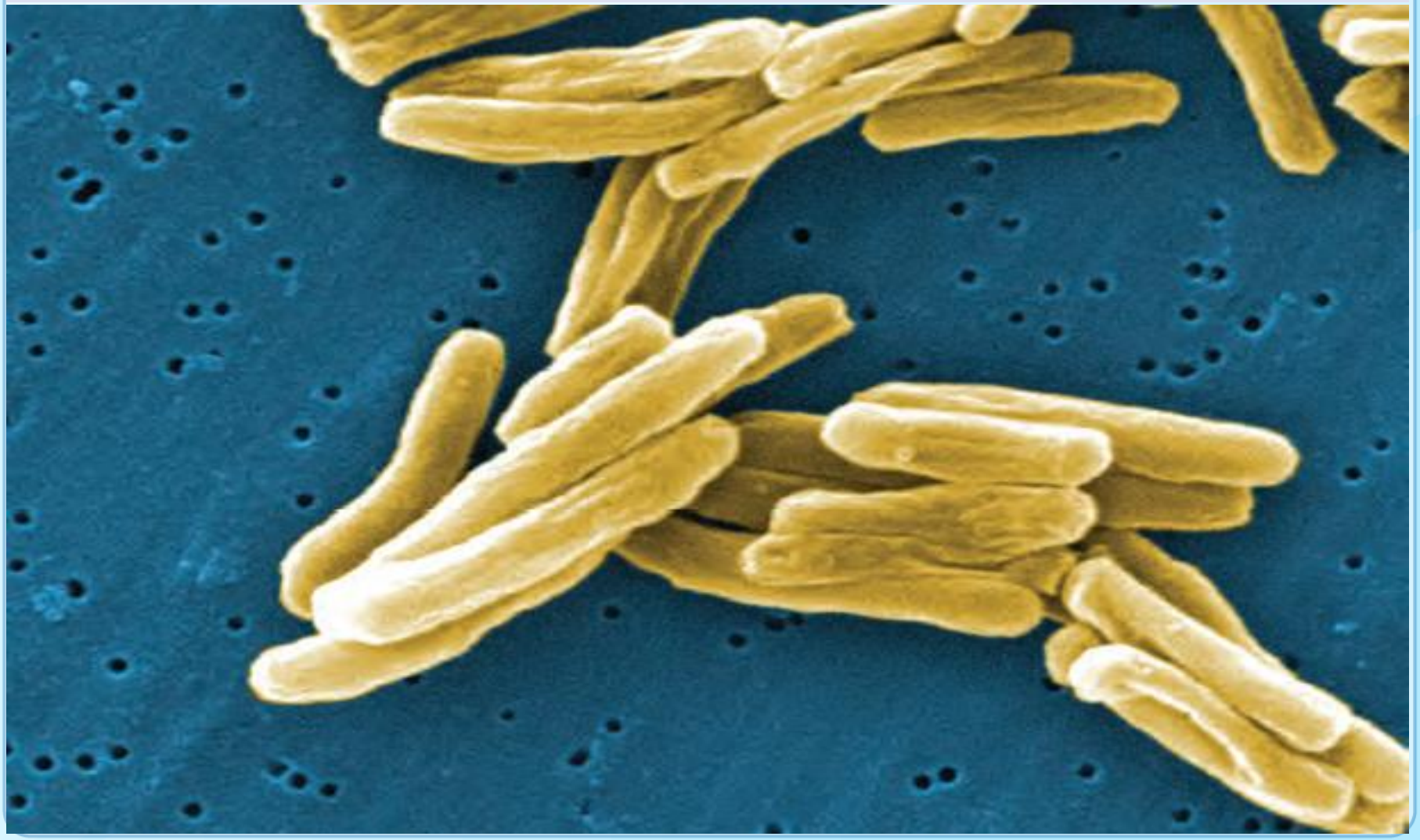
Introduction

- TB is an airborne disease caused by the bacterium *Mycobacterium tuberculosis* (*M. tuberculosis*) .
- *M. tuberculosis* and seven very closely related mycobacterial species (*M. bovis, M. africanum, M. microti, M. caprae, M. pinnipedii, M. canetti* and *M. mungi*) together comprise what is known as the *M. tuberculosis* complex. Most, but not all, of these species have been found to cause disease in humans. In the United States, the majority of TB cases are caused by *M. tuberculosis*. *M. tuberculosis* organisms are also called tubercle bacilli.



Epidemiology

- One fourth of the global population (approximately 2 billion persons) is estimated to be infected with *Mycobacterium tuberculosis* .
- More than 5.7 million new cases of TB (all forms, both pulmonary and extra- pulmonary) were reported to the World Health Organization (WHO) in 2013;95% of cases were reported from developing countries
- Globally, an estimated 10.0 million (range, 9.0–11.1 million) 2 people fell ill with TB in 2018
- Of further concern is that 480 000 cases of multidrug-resistant (MDR) TBa anda further 100 000 that were estimated to be rifampicin-resistant (RR) TB have occurred in the same period

- With the notable exception of sub-Saharan Africa, the incidence of tuberculosis has declined over the past two decades in most regions of the world.
- Tuberculosis remains one of the deadliest diseases in the world
- There were an estimated 1.2 million (range, 1.1–1.3 million) TB deaths among HIV-negative people in 2018

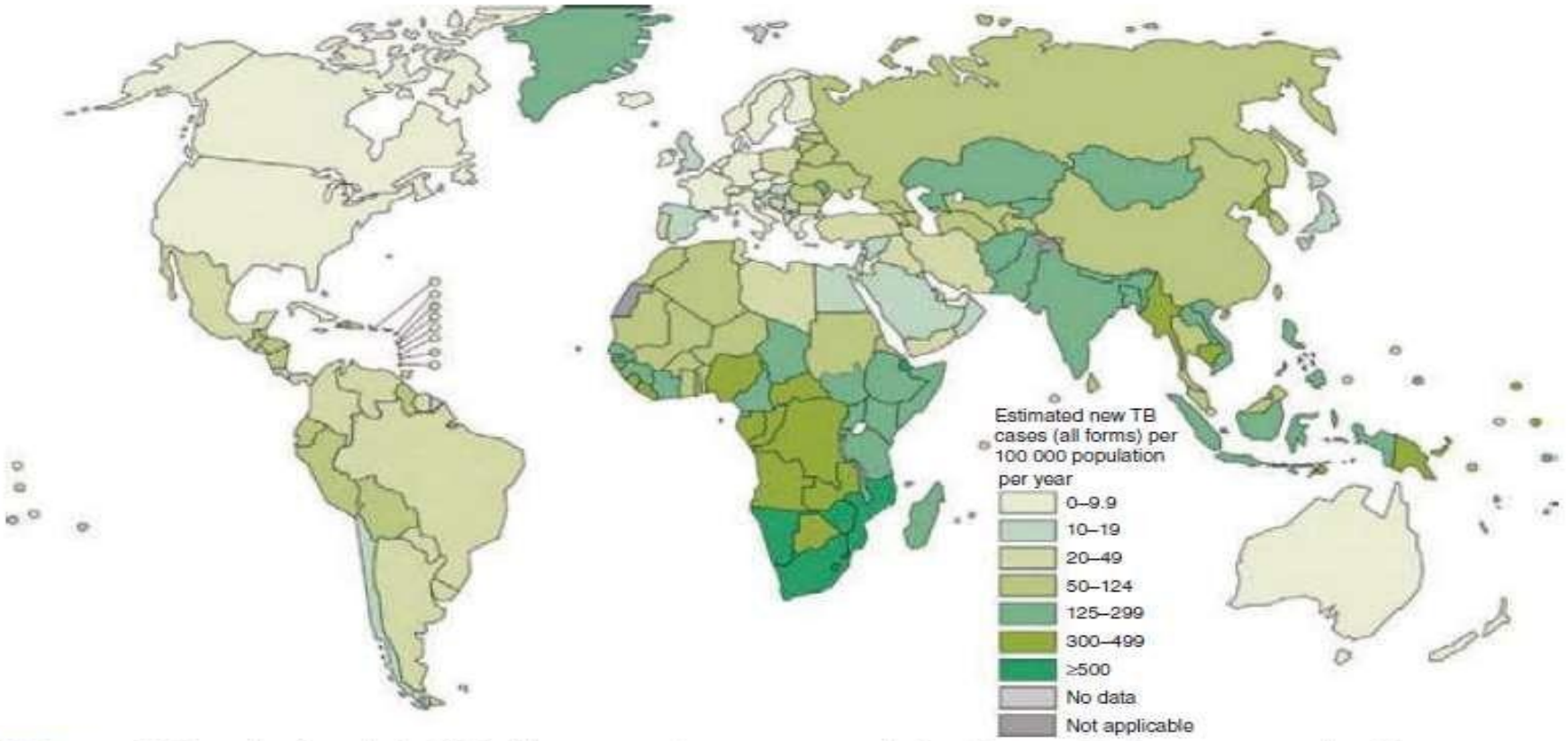


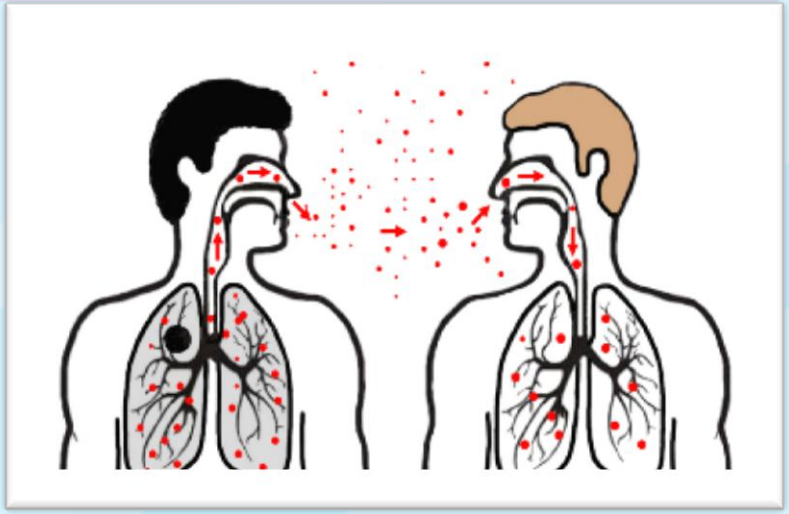
FIGURE 202-2 Estimated tuberculosis (TB) incidence rates (per 100,000 population) in 2013. The designations used and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization (WHO) concerning the legal status of any country, territory, city, or area or of its authorities or concerning the delimitation of its frontiers or boundaries. *Dotted*, *dashed*, and *white lines* represent approximate border lines for which there may not yet be full agreement. *(Courtesy of the Global TB Programme, WHO; with permission.)*

What about YEMEN???

- The disease is considered a major public health problem, ranking fourth on the list of public health priorities.
- In 2017, the World Health Organization (WHO) reported that Yemen had 13,000 new TB cases, with an incidence rate of 47 cases per 100,000 individuals

Transmission and Pathogenesis

- *M.TB* spread via airborne particles called droplet nuclei
- Expelled when person with infectious TB coughs, sneezes, shouts, or sings



- Transmission occurs when droplet nuclei inhaled and reach the alveoli of the lungs, via nasal passages, respiratory tract, and bronchi

Probability TB Will Be Transmitted

- Susceptibility of the exposed person(immune status)
- Infectiousness of person with TB (i.e., number of bacilli TB patient expels into the air)
- clinical (Presence of cough for 3WKS ,Respiratory tract disease, involvement of the larynx , NOT cover the mouth and nose when coughing Inappropriate treatment)
- Procedure(bronchoscopy, sputum induction, administration of aerosolized medications)
- Radiographic and laboratory
- Cavitation on chest radiograph
- Positive culture for M. tuberculosis
- Positive AFB sputum smear result

Probability TB Will Be Transmitted

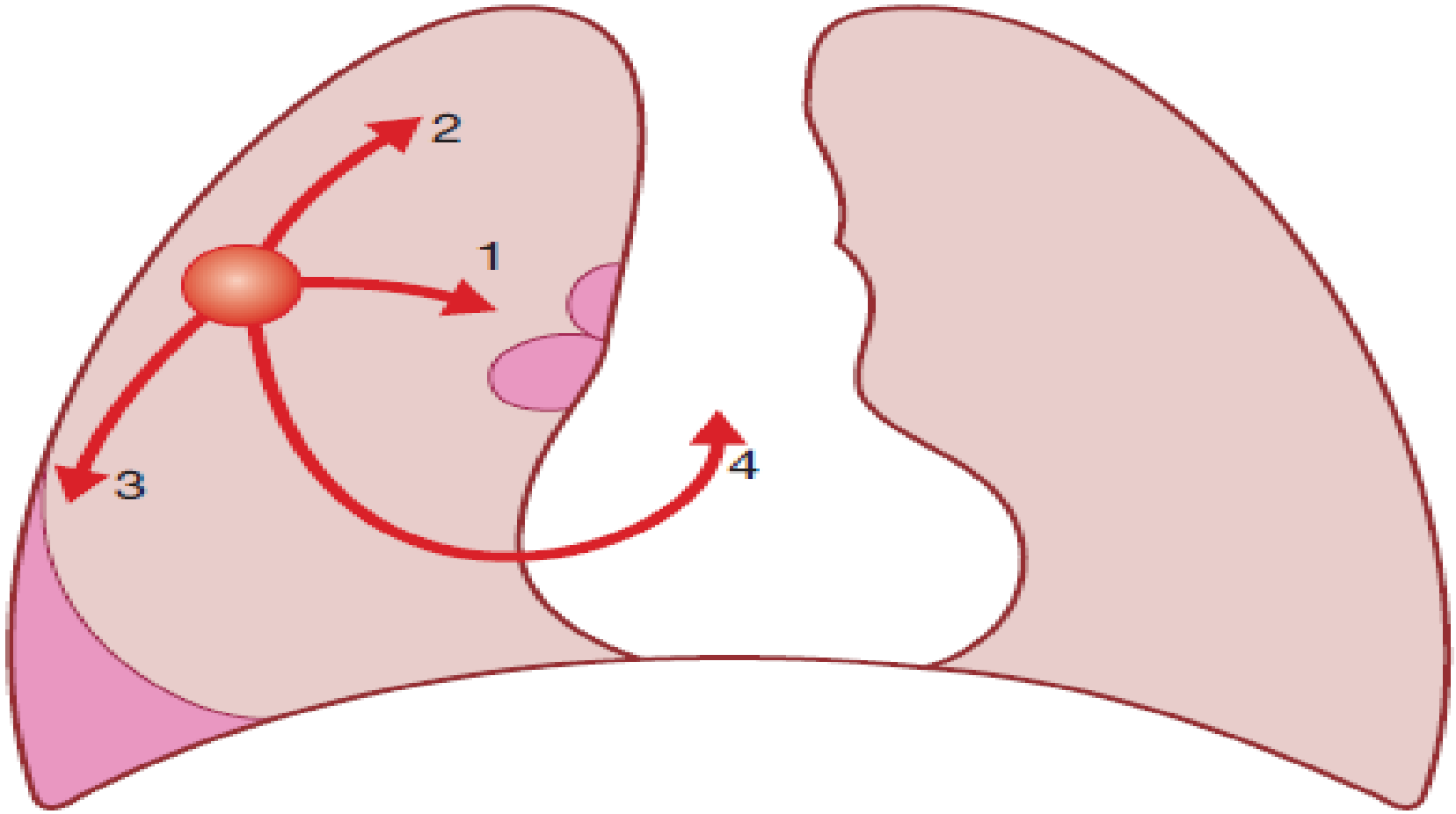
- Environmental factors that affect the concentration of M. tb organisms
- ✓ Concentration(more droplet nuclei in the air)
- ✓ small, enclosed spaces
- ✓ Inadequate local or general ventilation
- ✓ Recirculation of air
- ✓ Improper specimen handling
- ✓ Positive air pressure in Pt room
- Proximity, frequency, and duration of exposure (e.g., close contacts)
- Can be transmitted from children, though less likely

PATHOGENESIS

- Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to the alveoli
- Tubercle bacilli multiply in the alveoli
- recruitment of macrophages and lymphocytes
- Within 2 to 8 weeks, macrophages ingest and surround the tubercle bacilli. Transformed macrophages aggregate with lymphocytes forming a barrier shell, called a granuloma, that keeps the bacilli contained and under control (LTBI). Numerous granulomas aggregate to form a primary lesion or 'Ghon focus in periphery of lungs
- Spread of organisms to the hilar lymph nodes is followed by a similar pathological reaction, and the combination of the primary lesion+ regional lymph nodes is referred to as the 'primary complex of Ranke

PATHOGENESIS

- Lymphatic or haematogenous spread may occur before immunity is established, however, seeding secondary foci in other organs, including lymph nodes, serous membranes, meninges, bones, liver, kidneys and lungs, which may lie dormant for years.
- If the reparative processes fail, primary progressive disease ensues. Persons with TB disease are usually infectious and can spread bacteria to others
- Persons with LTBI are not infectious and do not spread organisms to others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Factors increasing the risk of tuberculosis

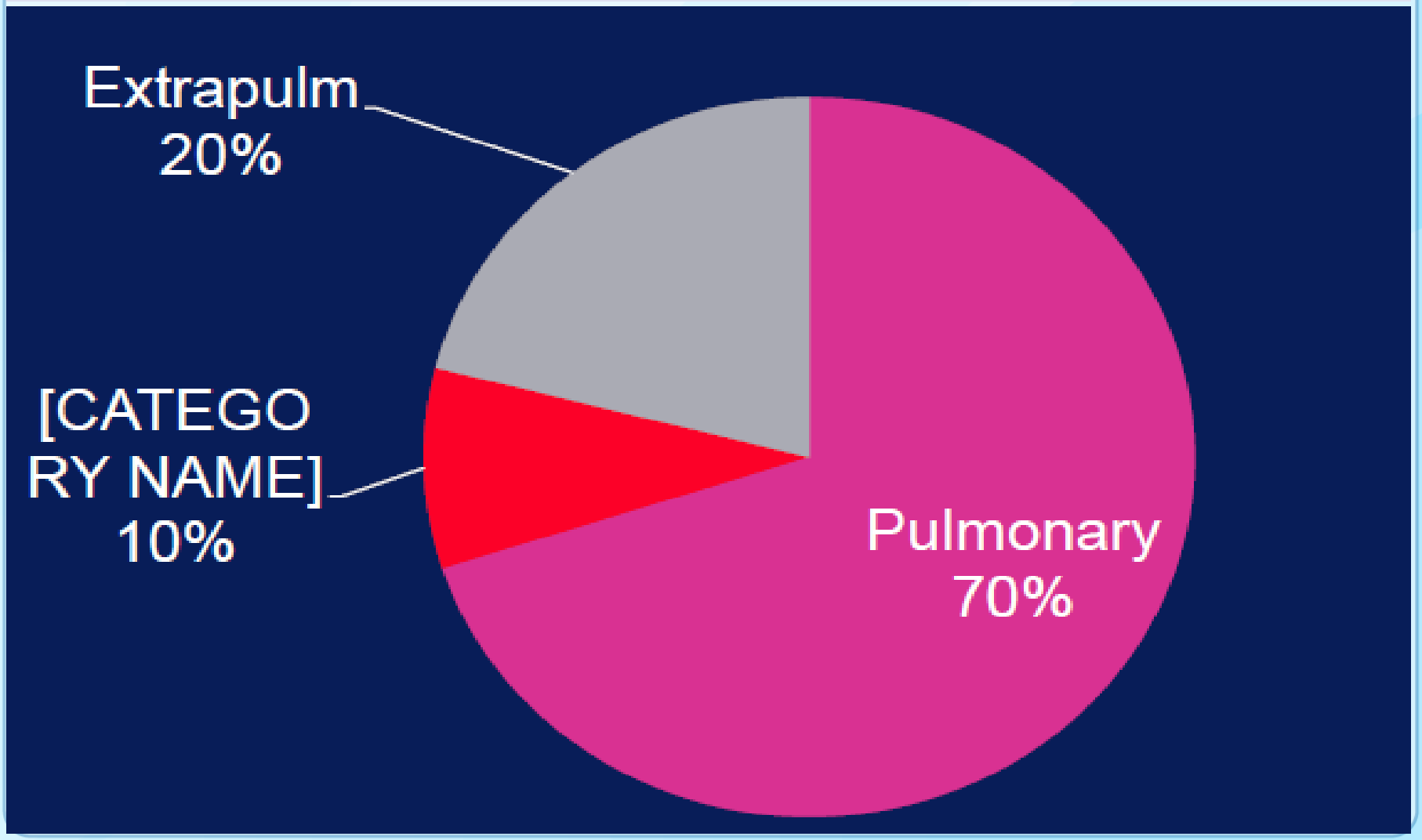
- **The estimated lifetime risk of developing disease after primary infection is 10%, with roughly half of this risk occurring in the first 2 years after infection.**

Patient-related
• Age (children > young adults < elderly) • First-generation immigrants from high-prevalence countries • Close contacts of patients with smear-positive pulmonary TB • Overcrowding (prisons, collective dormitories); homelessness (doss houses and hostels) • Chest X-ray evidence of self-healed TB • Primary infection < 1 yr previously • Smoking: cigarettes and bidis (Indian cigarettes made of tobacco wrapped in temburini leaves)
Associated diseases
• Immunosuppression: HIV, anti-tumour necrosis factor (TNF) therapy, high-dose corticosteroids, cytotoxic agents • Malignancy (especially lymphoma and leukaemia) • Diabetes mellitus • Chronic kidney disease • Silicosis • Gastrointestinal disease associated with malnutrition (gastrectomy, jejuno-ileal bypass, cancer of the pancreas, malabsorption) • Deficiency of vitamin D or A • Recent measles in children

CLINICAL MANIFESTATIONS OF TUBERCULOSIS

- The clinical manifestations of tuberculosis are quite variable and depend on a number of factors
- Host factors
  - age
  - Specificic immunodeficiency states
  - Malnutrition
  - Genetic factors (not yet defined)
  - Coexisting diseases
  - Immunization with bacillus Calmette-Guérin (BCG
- Virulence of the organism
- Sites of involvement,severity of disease

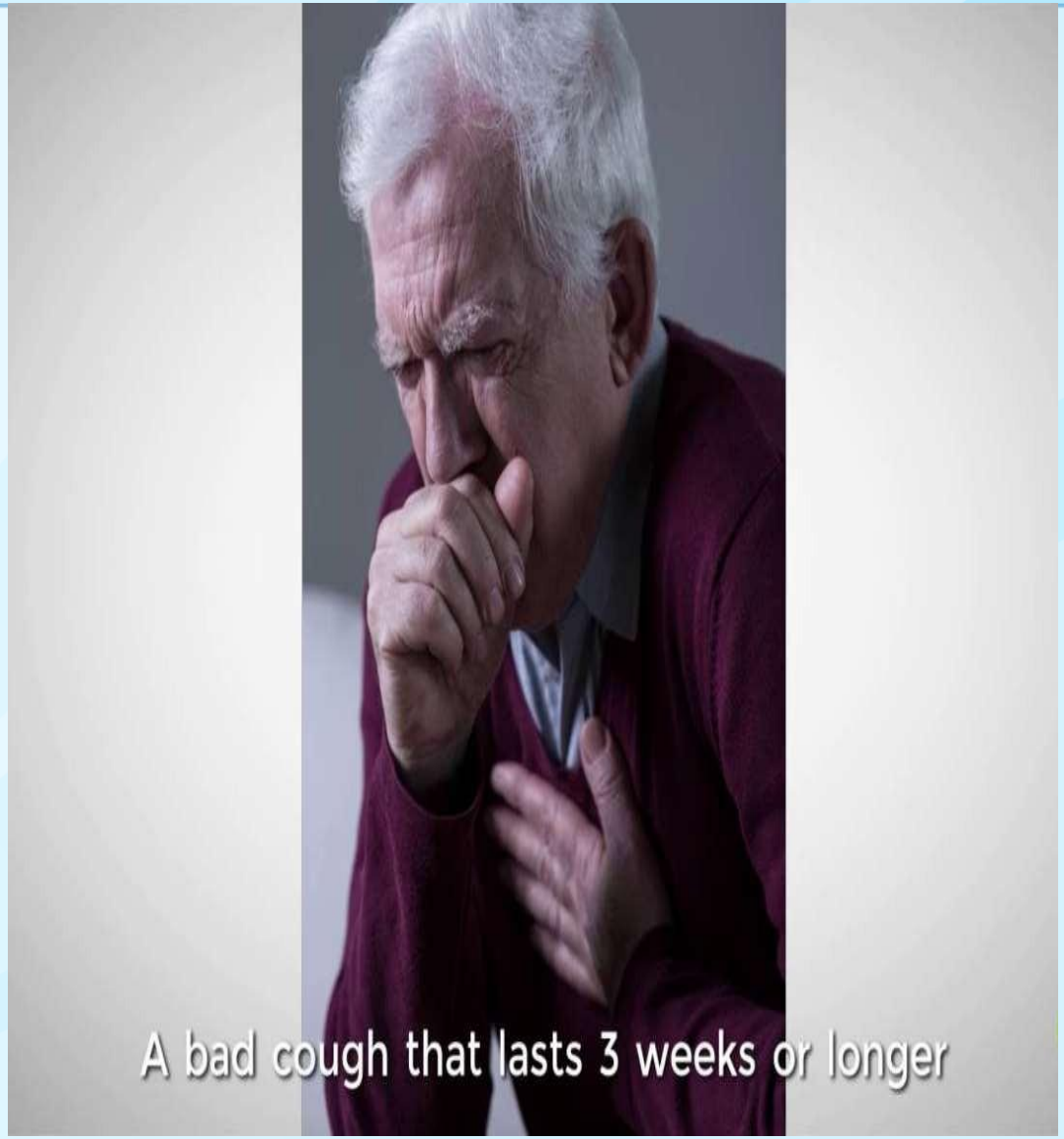
Sites of TB:
Pulmonary vs. Extrapulmonary



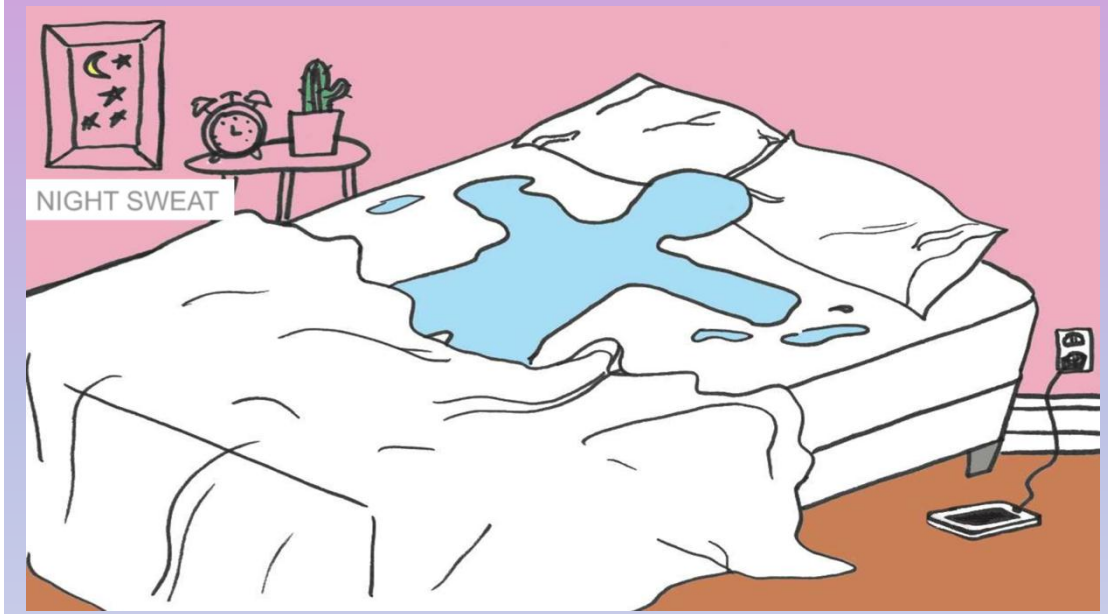
"Classic" Clinical Presentation of TB

- Insidious onset, chronic course
- Chest symptoms
- Cough (usually productive)
- Hemoptysis
- Chest pain (usually pleuritic)
- Nonspecific constitutional symptoms
- Extrapulmonary symptoms


HEMOPTYSIS

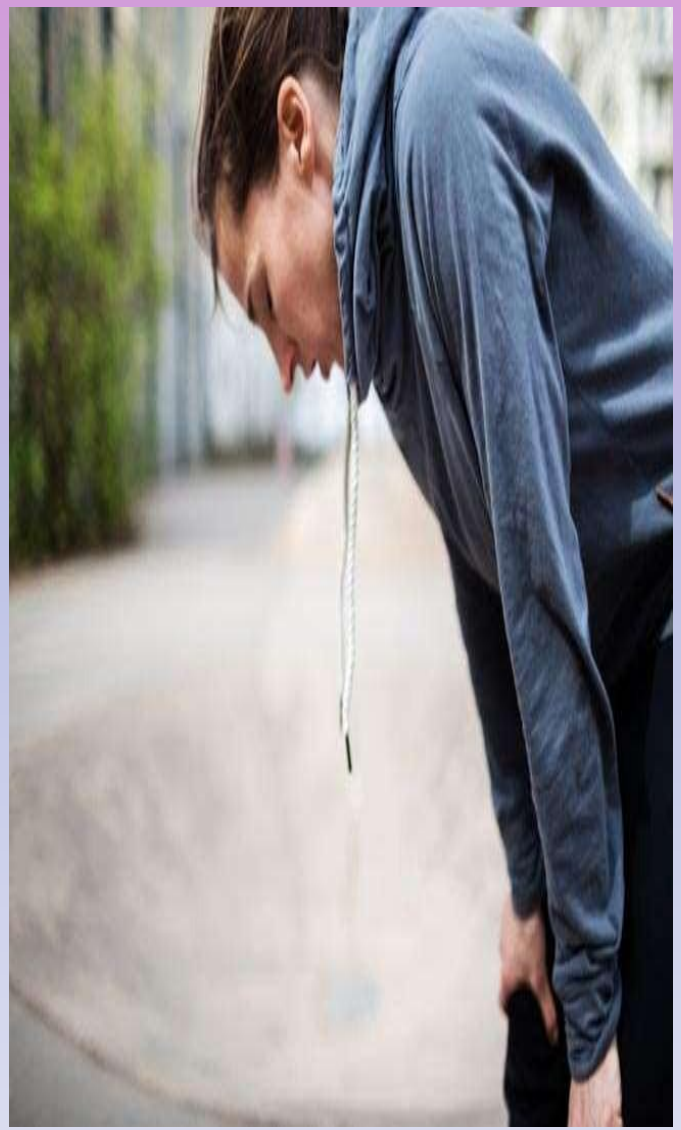

A bad cough that lasts 3 weeks or longer

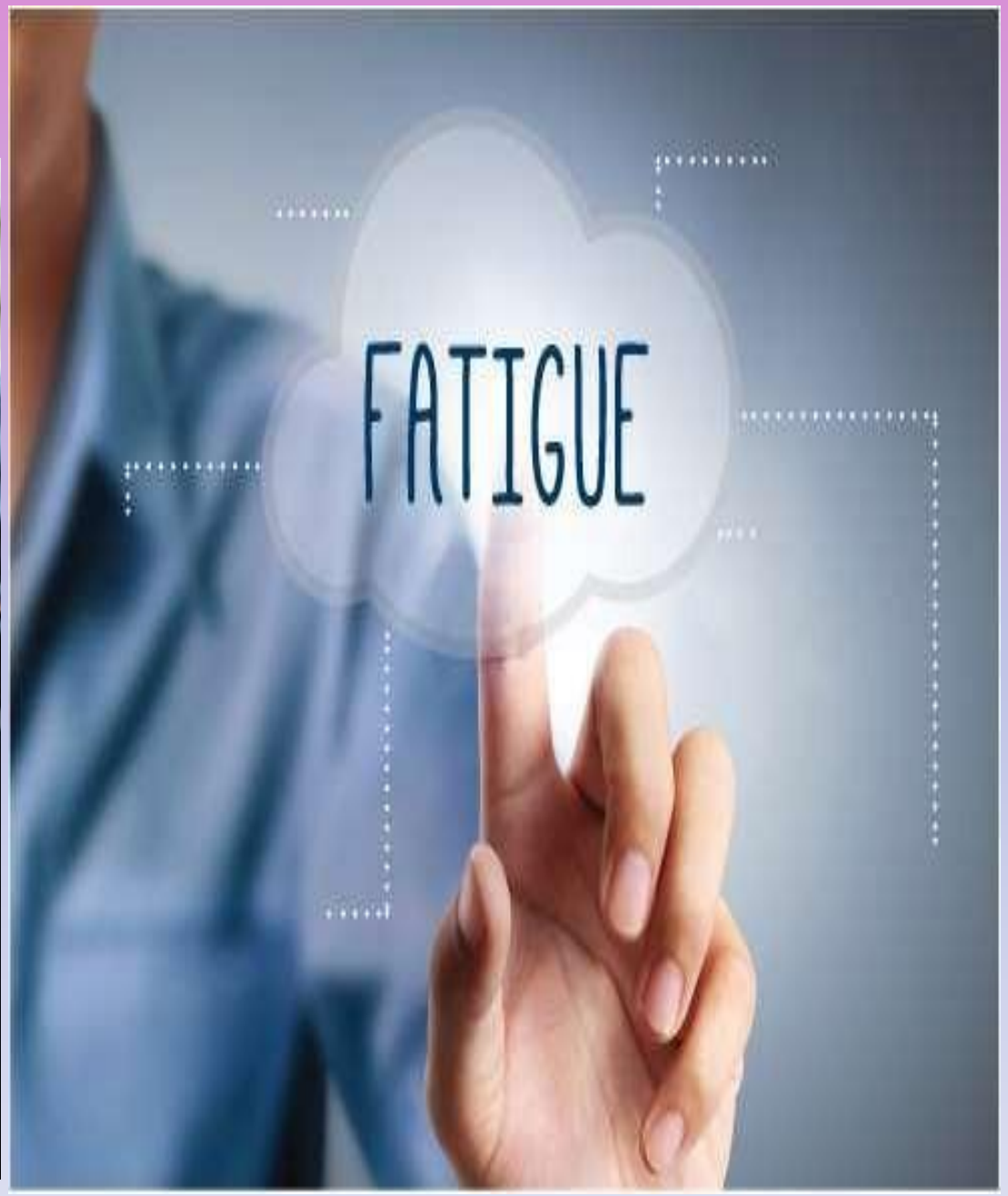
Weight loss



Loss of appetite

SOB





Clinical features: pulmonary disease

Primary pulmonary TB

- Primary TB refers to the infection of a previously uninfected (tuberculin-negative) individual.
- A few patients develop a self limiting febrile illness but clinical disease occurs only if there is a hypersensitivity reaction or progressive infection.
- Progressive primary disease may appear during the course of the initial illness or after a latent period of weeks or months

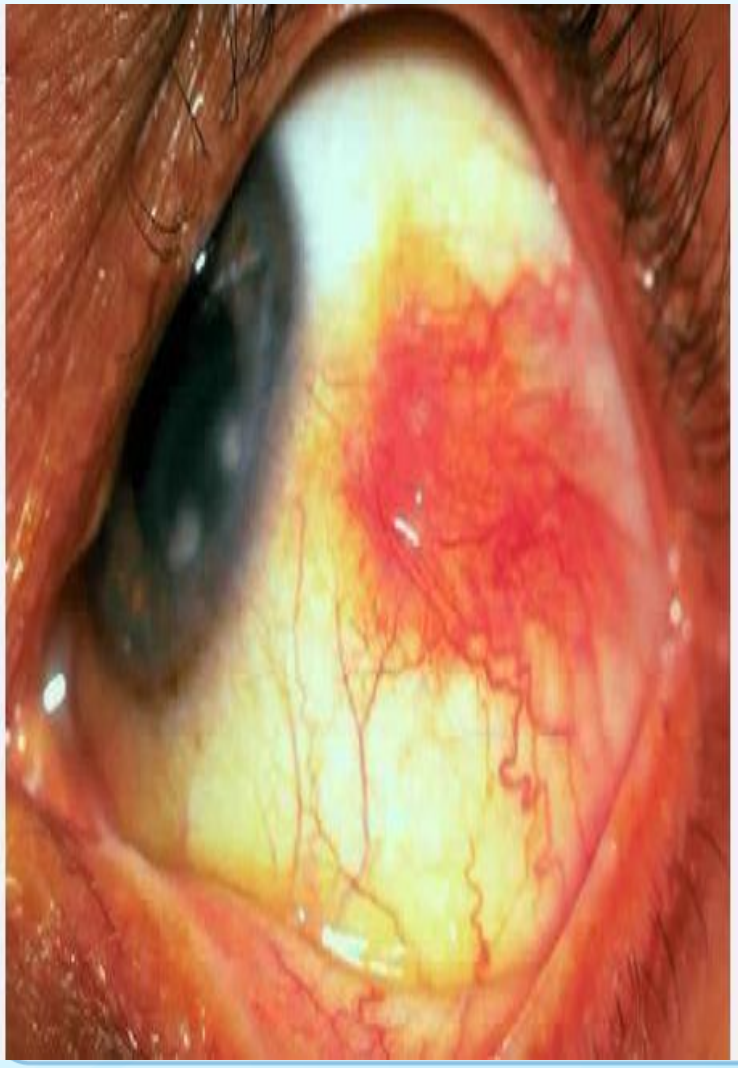
Features of primary tuberculosis

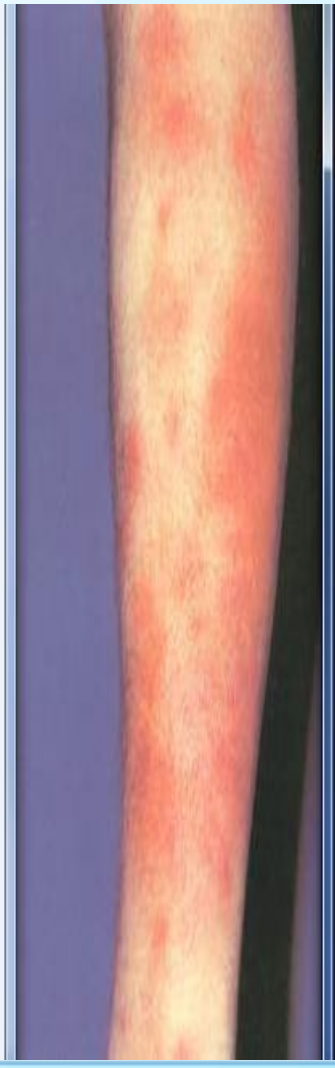
Infection (4–8 wks)	
• Influenza-like illness • Skin test conversion	• Primary complex
Disease	
• Lymphadenopathy: hilar (often unilateral), paratracheal or mediastinal • Collapse (especially right middle lobe) • Consolidation (especially right middle lobe)	• Obstructive emphysema • Cavitation (rare) • Pleural effusion • Miliary • Meningitis • Pericarditis
Hypersensitivity	
• Erythema nodosum • Phlyctenular conjunctivitis	• Dactylitis

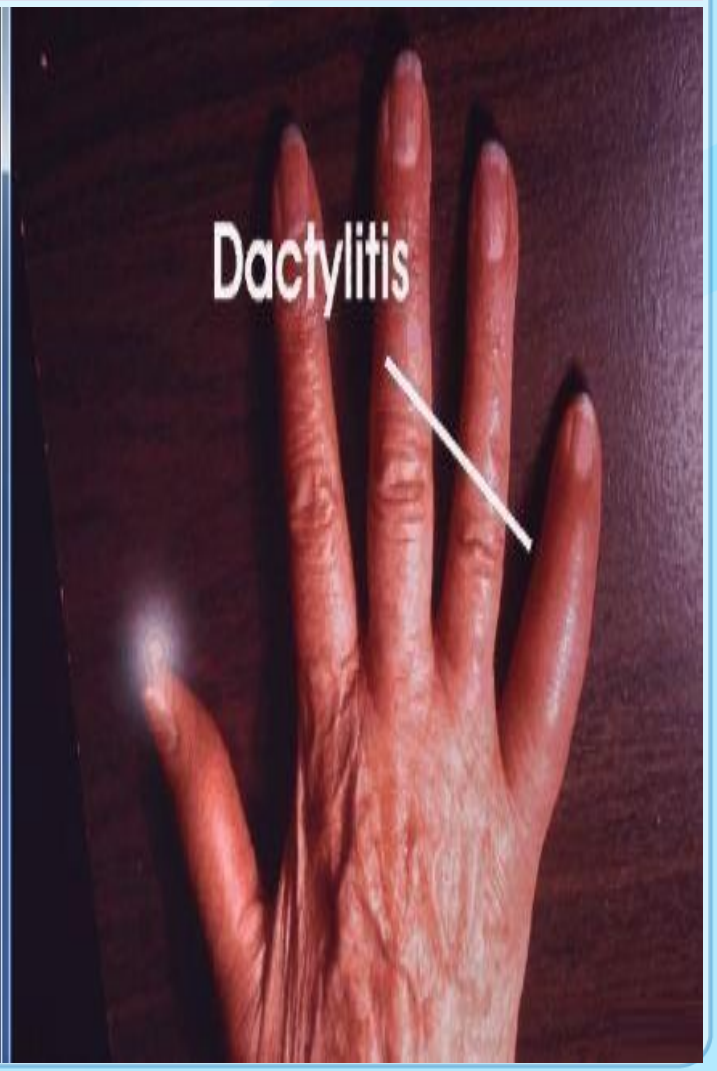
Natural history of untreated primary tuberculosis

Time from infection	Manifestations
3–8 wks	Primary complex, positive tuberculin skin test
3–6 mths	Meningeal, miliary and pleural disease
Up to 3 yrs	Gastrointestinal, bone and joint, and lymph node disease
Around 8 yrs	Renal tract disease
From 3 yrs onwards	Post-primary disease due to reactivation or re-infection

Features of primary tuberculosis







Disseminated tuberculosis(miliary)

- Disseminated tuberculosis occurs because of the inadequacy of host defenses in containing tuberculous infection. This failure of containment may occur in either latent or recently acquired tuberculous infection. Becauseof HIV or other causes of immunosuppression, the organism proliferates and disseminates throughout the body.
- Which may present acutely but more frequently is characterised by 2–3 weeks of fever, night sweats, anorexia, weight loss and a dry cough.
- Headache and mental status changes are less frequent and are usually associated with meningeal involvement (49).

Disseminated tuberculosis(miliary)

- Physical findings likewise are variable. Fever, wasting, hepatomegal,pulmonary findings, lymphadenopathy, and splenomegaly occur in descending order of frequency.
- A finding that is strongly suggestive of disseminated tuberculosis is the choroidal tubercle, a granuloma located in the choroid of the retina.
- Anaemia and leucopenia reflect bone marrow involvement.

Cryptic tuberculosis

- ‘Cryptic’ miliary TB is an unusual presentation sometimes seen in old age.
- Age over 60 years
- Intermittent low-grade pyrexia of unknown origin
- •Unexplained weight loss, general debility (hepatosplenomegaly in 25–50%)
- Normal chest X-ray
- Blood dyscrasias; leukaemoid reaction, pancytopenia
- Negative tuberculin skin test
- Confirmation by biopsy with granulomas and/or acid-fast bacilli in liver or bone marrow

Post-primary pulmonary TB

- Post-primary disease refers to exogenous ('new' infection) or endogenous (reactivation of a dormant primary lesion) infection in a person who has been sensitised by earlier exposure.
- The onset is usually insidious, developing slowly over several weeks. Systemic symptoms include fever, night sweats, malaise and loss of appetite and weight, and are accompanied by progressive pulmonary symptoms.
- Cough is the most common symptom of pulmonary tuberculosis. Early in the course of the illness it may be nonproductive, but subsequently, as inflammation
- and tissue necrosis ensue, sputum is usually produced
- and is key to most of our diagnostic methods. sis)

Post-primary pulmonary TB

- Hemoptysis may rarely be a presenting symptom but usually is the result of previous disease and does not necessarily indicate active tuberculosis.
- Hemoptysis may result from residual tuberculous bronchiectasis, rupture of a dilated vessel in the wall of a cavity (Rasmussen's aneurysm), bacterial or fungal infection (especially Aspergillus in the form of a mycetoma) in a residual cavity, or from erosion of calcified lesions into the lumen of an airway (broncholithiasis)
- may pleuritic pain, Dyspnea is unusual unless there is extensive disease. severe respiratory failure or symptoms of complications

Post-primary pulmonary TB

- Occasionally, a caseous lymph node may drain into an adjoining bronchus, leading to tuberculous pneumonia
- Others presentations may include
  - Pyrexia of unknown origin
  - Exudative pleural effusion
  - Asymptomatic (diagnosis on chest X-ray)
  - Spontaneous pneumothorax
- Physical findings in pulmonary tuberculosis are not generally helpful in defining the disease. Rales may be heard in the area of involvement as well as bronchial breath sounds in upper lobes if there is lung consolidation.

Post-primary pulmonary TB

	Sensitivity
Cough (dry/productive sputum)	75-80%
Weight loss	45-75%
Fatigue	60-70%
Fever	50-60%
Night sweats	50-55%
Hemoptysis	25-35%
No symptoms	10-20%

Complications of chronic pulmonary tuberculosis

Pulmonary

- Massive haemoptysis
- Cor pulmonale
- Fibrosis/emphysema
- Atypical mycobacterial infection
- Aspergilloma
- Lung/pleural calcification
- Obstructive airways disease
- Bronchiectasis
- Bronchopleural fistula

Non-pulmonary

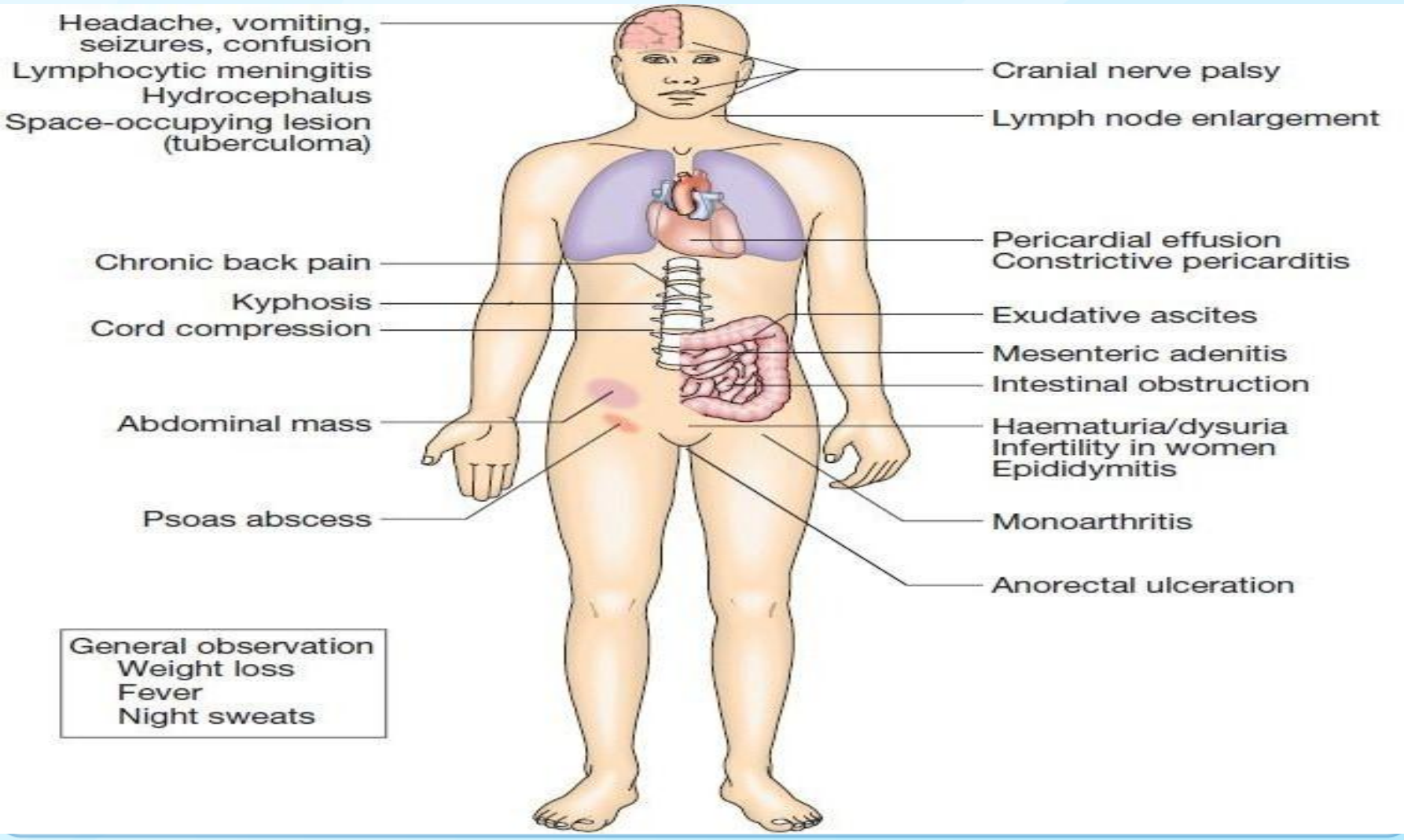
- Empyema necessitans
- Laryngitis
- Enteritis*
- Anorectal disease*
- Amyloidosis
- Poncet's polyarthritis

*From swallowed sputum.

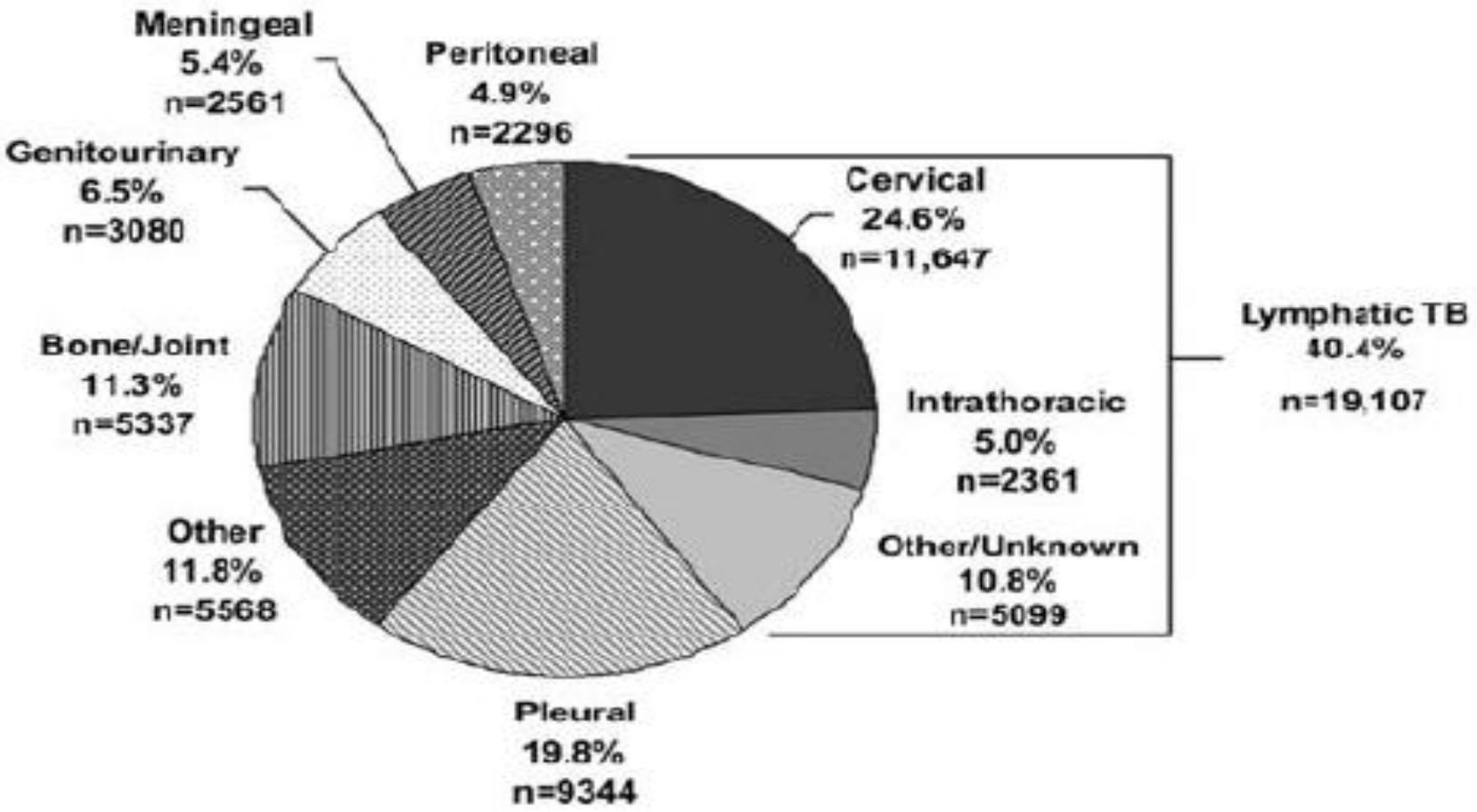
Extrapulmonary tuberculosis

- Extrapulmonary TB accounts for 20% of cases in those who are HIV-negative but is more common in HIV-positive patients.
- Extrapulmonary tuberculosis usually presents more of a diagnostic problem than pulmonary tuberculosis.

Extrapulmonary tuberculosis



Extrapulmonary tuberculosis



Lymphadenitis

- Disease may represent primary infection, spread from contiguous sites or reactivation
- Lymph nodes are the most common extrapulmonary site of disease. Cervical and mediastinal glands are affected most frequently, followed by axillary and inguinal, and more than one region may be involved...
- The nodes are usually painless and initially mobile but become matted together with time. When caseation and liquefaction occur, a 'collar-stud' abscess and sinus formed.
- 50% no constitutional features, such as fever
- Pulmonary involvement, ranging from 5 to 70%
- The tuberculin test is usually strongly positive. paradoxical enlargement During tt may occur or after

Pleural tuberculosis.

- **Pleural effusion**
- Immune mediated(small no of bacilli, Commonly, this form of tuberculous pleuritis goes unnoticed)
- **Direct involvement of pleura**
- an acute illness with fever and pleuritic pain. If the effusion is large enough, dyspnea may occur, although the effusions generally are small and rarely are bilateral. In approximately 30%of patients there is no radiographic evidence of involvement of the lung parenchyma
- **Empyema**
- much less common ,results from a large number of organisms spilling into the pleural space, usually associated with evident pulmonary parenchymal disease on ches films and air may be seen in the pleural space

Gastrointestinal tuberculosis

- TB can affect any part of the bowel and patients may presentwith a wide range of symptoms and signs.
- Upper GITinvolvement is rare
- The most common sites of involvement are the terminal ileum and cecum(50%), with other portions of the colon and the rectum involved less frequently.
- In the terminal ileum or cecum the most common manifestations are pain, which may be misdiagnosed as appendicitis, and intestinal obstruction(acute abd in 30%).
- Fever, night sweats, anorexia and weight loss are usually prominent and a right iliac fossa mass may be palpable

- Rectal lesions usually present as anal fissures, fistulae, or perirectal abscesses
- Tuberculous peritonitis
- frequently causes pain as its presenting manifestation, often accompanied by abdominal swelling
- Fever, weight loss, and anorexia are also common.
- Active pulmonary tuberculosis is uncommon.
- **The combination of fever and abdominal tenderness in a person with ascites should always prompt an evaluation for intraabdominal infection, and a paracentesis should be performed.** However, this is often not diagnostic, and laparoscopy with biopsy is recommended if tuberculosis is suspected

Pericardial disease

- Disease occurs in two forms : pericardial effusion and constrictive pericarditis.
- the presentation is usually insidious, Fever, weight loss, and night sweats are common .
- Symptoms of cardiopulmonary origin tend to occur later and include cough, dyspnea, orthopnea, ankle swelling, and chest pain, abdominal swelling. Coexistent pulmonary disease is very rare, with the exception of pleural effusion.
- Physical signs include Pulsus paradoxus, a raised JVP, hepatomegaly, prominent ascites and peripheral oedema Increased pericardial dullness and third heart sound ,AF
- Consider TB if 4C(, constitutional,color(red),calcifications (30%) ,constrictitive)

Central nervous system tuberculosis.

- 2 forms TB meningitis or tuberculoma
- Tuberculous meningitis
- Tuberculous meningitis most commonly occurs shortly after a primary infection in childhood or as part of miliary tuberculosis.
- The usual local source of infection is a caseous focus in the meninges or brain substance adjacent to the CSF pathway
- In tuberculous meningitis the process is located primarily at the base of the brain.
- If untreated, tuberculous meningitis is fatal in a few weeks but complete recovery is usual if treatment is started at stage I When treatment is initiated later, the rate of death or serious neurological deficit may be as

Clinical features and staging of tuberculous meningitis

- **Onset is much slower than in other bacterial meningitis – over 2–8 weeks**

Symptoms

- Headache
- Vomiting
- Low-grade fever
- Lassitude
- Depression
- Delirium
- Behaviour changes

Signs

- Meningism (may be absent)
- Oculomotor palsies
- Papilloedema
- Depression of conscious level
- Focal hemisphere signs

Staging of severity

- Stage I (early): non-specific symptoms and signs without alteration of consciousness
- Stage II (intermediate): altered consciousness without coma or delirium *plus* minor focal neurological signs
- Stage III (advanced): stupor or coma, severe neurological deficits, seizures or abnormal movements

- In most series more than 50% of patients with meningitis have abnormalities on chest film
- lumbar puncture is usually the next step in the diagnostic sequence or after CT scan if indicated.
- **The tuberculoma**
- presents a more subtle clinical picture than tuberculous meningitis .The usual presentation is that of a slowly growing focal lesion, although a few patients have increased intracranial pressure and no focal findings.
- The cerebrospinal fluid is usually normal, and the diagnosis is established by computed tomographic or magnetic resonance scanning and subsequent resection, biopsy, or aspiration of any ring-enhancing lesion

Bone and joint disease

- bone involvement with tuberculosis is much more common in children than adults.
- Th spine
- e the most common site for bony TB (Pott's disease), which usually presents with chronic back pain and typically involves the lower thoracic and lumbar spine The infection starts as a discitis and then spreads along the spinal ligaments to involve the adjacent anterior vertebral bodies, causing kyphosis.
- Paravertebral and psoas abscess formation is common and the disease may present with a large (cold) abscess in the inguinal region. CT or MRI is valuable in gauging the extent of disease. Systemic symptoms of infection are not common.,MAY LEAD to cord compression

Bone and joint disease

- **Joint s**
- **TB can affect any joint but most frequently involves the hip or knee or ankle .**
- **Presentation is usually insidious,monoarthritis or oligoarthritis with pain and swelling.**
- **fever and night sweats are uncommon.**
- **Radiological changes are often non-specific but, as disease progresses, reduction in joint space and erosions appear.**
- **Poncet's arthropathy immunologically mediated polyarthritis that usually resolves within 2 months of starting treatment.**

Genitourinary tuberculosis

- Local symptoms predominate and systemic symptoms
- Are less common . Dysuria, hematuria, and frequent
- urination are common, and flank pain may also be noted. However, the symptoms may be subtle, and, often, there is advanced destruction of the kidneys by the time a diagnosis is established . In women genital involvement is more common without renal tuberculosis than in men and may cause pelvic pain, menstrual irregularities, and infertility as presenting complaints In men a painless or only slightly painful scrotal mass is probably the most common presenting symptom of genital involvement, but symptoms of prostatitis, orchitis, or epididymitis .
- **The finding of pyuria in an acid urine with no routine bacterial organisms isolated from a urine culture should prompt an evaluation for tuberculosis by urine culture**

Evaluation and diagnosis of TB

- Medical history
- Physical examination
- Bacteriologic examination
- Radiology
- Test for TB infection

Bacteriologic examination

- Examinations of clinical specimens (e.g., sputum, urine, or cerebrospinal fluid) are of critical diagnostic importance. The specimens should be examined and cultured in a laboratory that specializes in testing for M. tuberculosis.
- The bacteriologic examination includes:

✓ Specimen collection, processing, and review

✓ AFB smear classification and results

✓ Specimen culturing and identification

✓ Direct detection of M. tuberculosis in clinical specimen using nucleic acid amplification (NAA)

✓ Drug-susceptibility testing

Bacteriologic examination

Specimens required

Pulmonary

- Sputum* (induced with nebulised hypertonic saline if not expectorating)
- Bronchoscopy with washings or BAL
- Gastric washing* (mainly used for children)

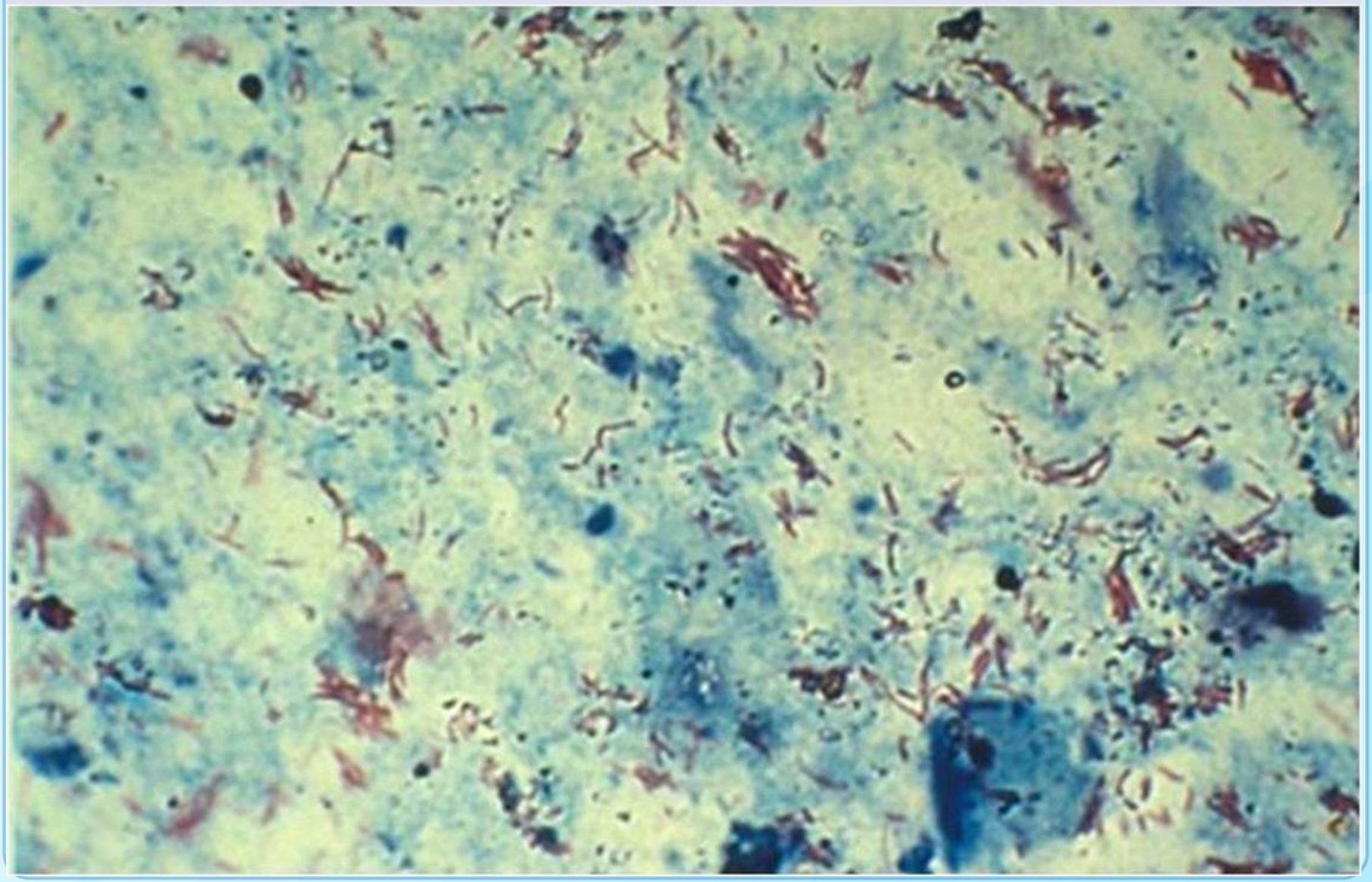
Extrapulmonary

- Fluid examination (cerebrospinal, ascitic, pleural, pericardial, joint): yield classically very low
- Tissue biopsy (from affected site): bone marrow/liver may be diagnostic in disseminated disease

Sputum examination

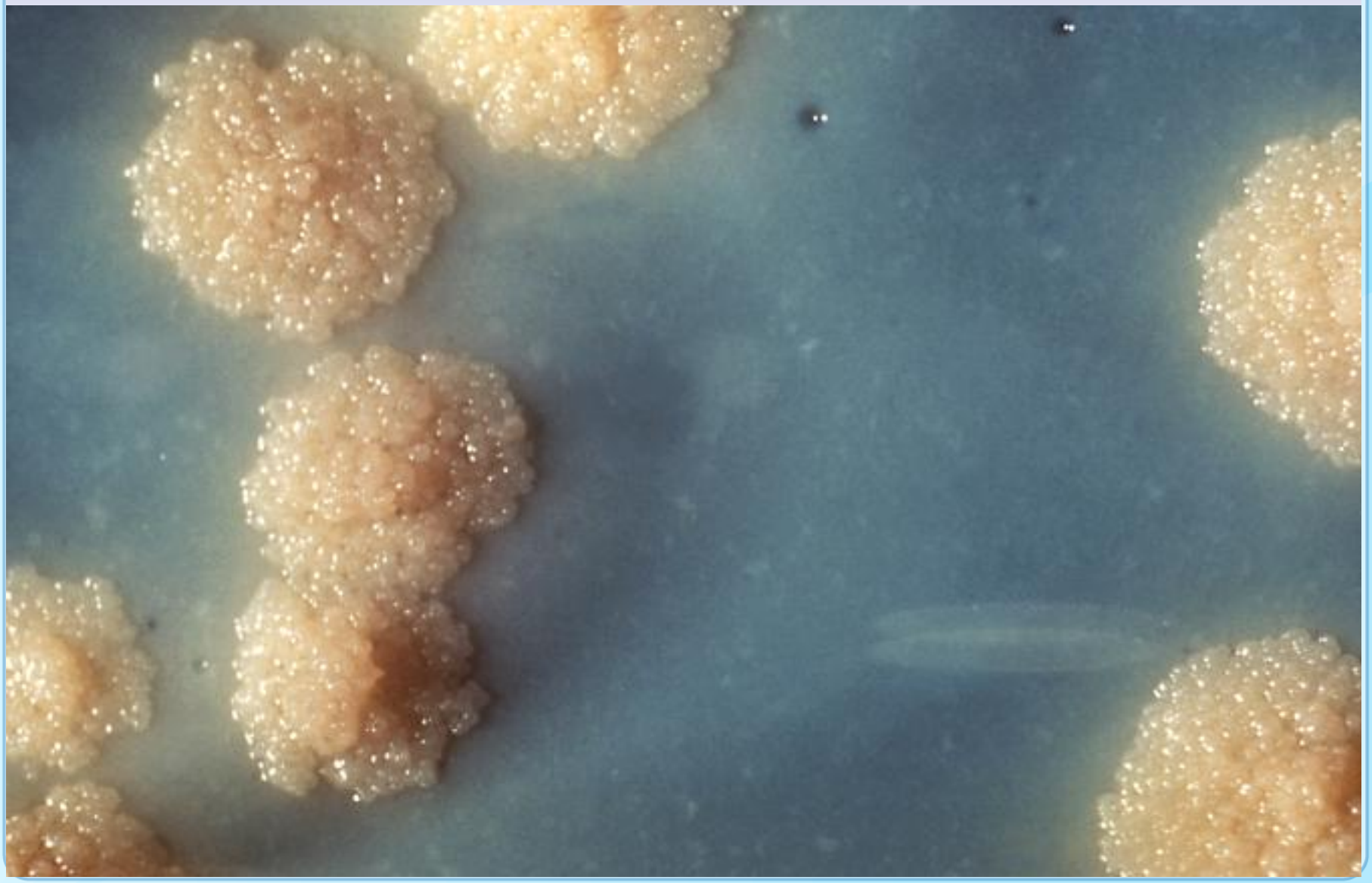
- For diagnostic purposes, all persons suspected of having TB disease (any where) should have sputum collected for AFB smear and culture.
- At least two but preferably three, including an early morning sample with interval 8hr-24hrs
- Detecting AFB in smears may be first evidence of mycobacteria
  - Quickest (results within 24 hours) and easiest procedure
  - Provides a preliminary presumptive diagnosis of TB
  - AFB in a smear are counted and classified as 4+, 3+, 2+, or 1+
- Sensitivity in pulmonary TB 50-60% increased to 70% with 3rd sample
- Negative test doesn't exclude diagnosis

- There are two procedures commonly used for acid-fast staining:
- Carbolfuchsin methods which include the Ziehl-Neelsen and Kinyoun methods(direct microscopy)
- Fluorochrome procedure using auramine-O or auramine-rhodamine dyes (fluorescent microscopy).
- Studies have shown that there must be 5,000 to 10,000 bacilli per milliliter of specimen to allow the detection of bacteria in stained smears



Specimen Culture and Identification

- Remains gold standard for confirming diagnosis of TB
- Culture all specimens, even if smear or NAA negative
- Medias used
  - Solid media (3–8 wk)
    - ✓ egg based (Löwenstein–Jensen) better detection slightly
    - ✓ agar based (Middlebrook 7H10,7H11) rapid detection
  - Liquid media (Middlebrook 7H12)(10-14 days)
  - Automated culture systems((radiometric or colorimetric systems) (4-10 days)
    - ✓ as BACTEC 460 (, Sparks, MD),(MGIT)
- sensitivity (80%-85%)
- **Negative culture dosnt exclude TB**
- Also used to assess infectivity ,response of treatment



Nucleic acid amplification tests (NAAT)

- NAA tests rapidly identify M. tuberculosis in a specimen via DNA and RNA amplification
- Benefits may include
- ✓ Earlier lab confirmation of TB disease
- ✓ Earlier respiratory isolation and treatment initiation
- ✓ Improved patient outcomes; interruption of transmission
- FDA-approved direct amplification tests Gen-Probe/MTD and Xpert Mtb/RIF
- Sensitivity for pulmonary TB (75-80%)
- negative result dosnt exclude TB

Drug-Susceptibility Testing

- For all patients, the initial M. tuberculosis isolate should be tested for resistance to the first-line anti-TB drugs
- Repeat for patients who
- Do not respond to therapy or
- Have positive cultures despite 3months of therapy
- Second-line Drug-Susceptibility Testing
- Limit to persons at increased risk for drug resistance:
- Have history of treatment with TB drugs
- Had contact with a person with drug-resistant TB
- Demonstrated resistance to first-line drugs
- Has positive smears or cultures despite 3 months of TB treatment

Molecular Detection of Drug Resistance and genotyping

- Drug resistance is caused by mutations in specific M. tb genes
- Several molecular assays and tests can detect mutations
- Genotyping
  - Laboratory-based approach that analyzes the genetic material of patient isolates
  - Main purpose of genotyping: add to TB controllers' understanding of TB transmission in their community

Test for M. tuberculosis Infection

- Currently, there are two methods available for the detection of M. tuberculosis infection .
- The tests are:
- Mantoux tuberculin skin test (TST)
- Interferon-gamma release assays (IGRAs)*
  - QuantiFERON-TB Gold In-Tube test (QFT-GIT)
  - T-SPOT®.TB test
- TST and QFT tests help clinicians differentiate people infected with M. tuberculosis from those uninfected. However, a negative reaction to any of the tests does NOT exclude the diagnosis of TB disease or LTBI.
- They don't differentiate active TB from latent TB
- More useful in extrapulmonary TB

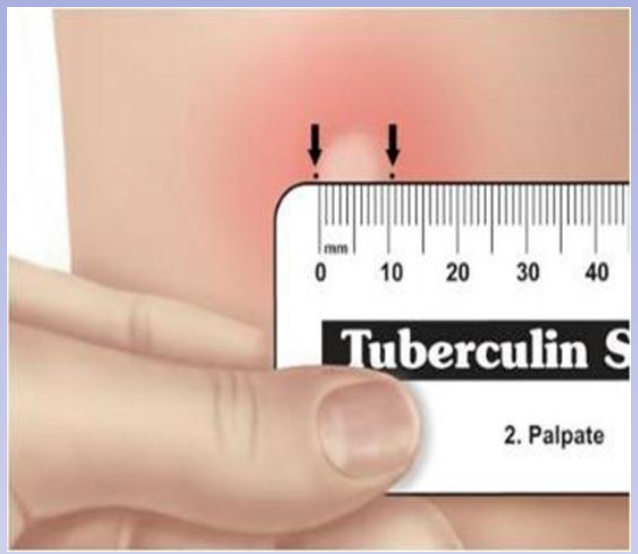
Mantoux tuberculin skin test (TST)

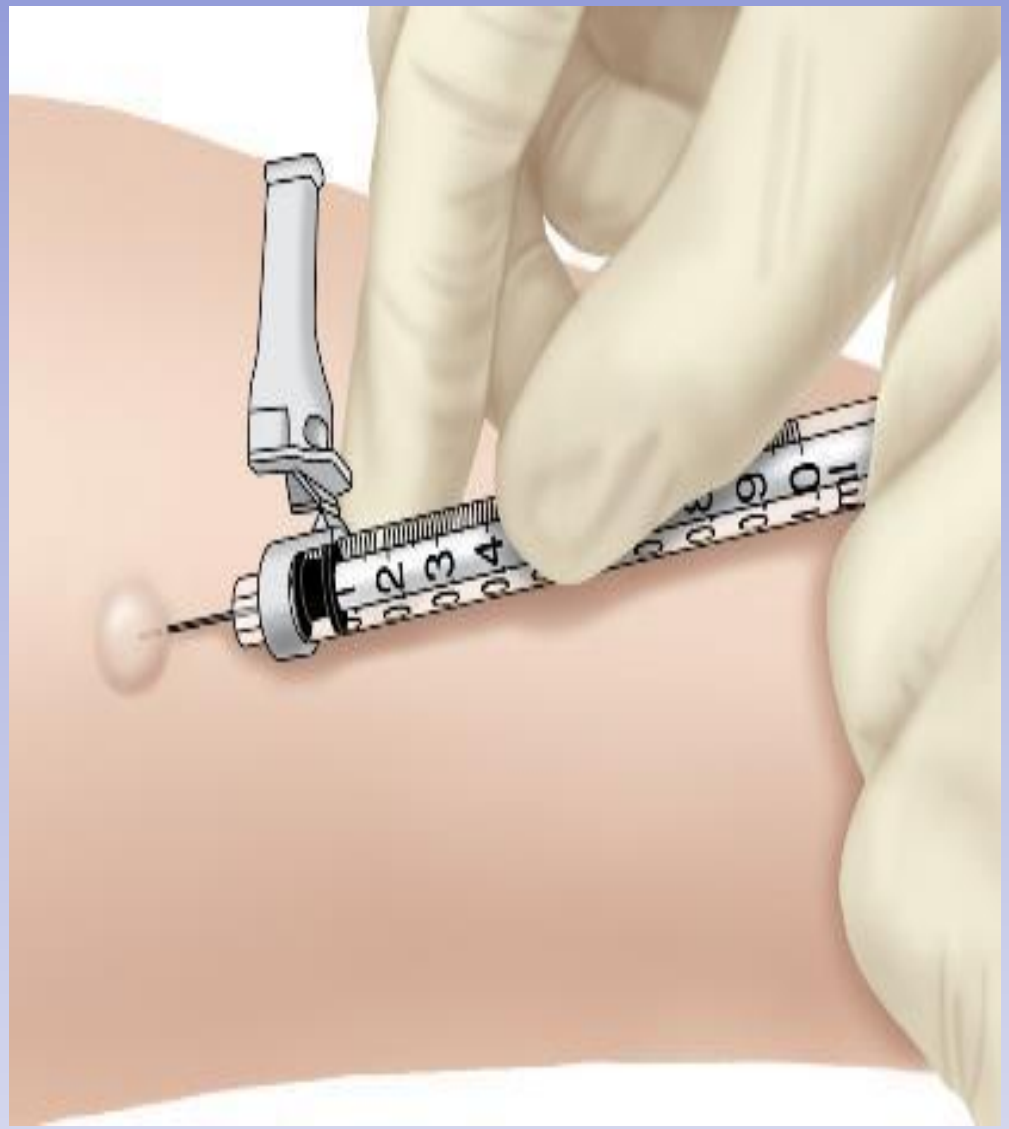
- Immunologic Basis for the Tuberculin Reaction
- The reaction to intracutaneously injected tuberculin is the classic example of a delayed (cellular) hypersensitivity reaction.
- T cells sensitized by prior infection are recruited to the skin site where they release lymphokines (127). These lymphokines induce induration through local vasodilatation, edema, fibrin deposition.
- Features of the reaction include (1) its delayed course, the reaction to tuberculin begins 5 to 6 h after injection, causes maximal induration at 48 to 72 h, and subsides over a period of days; (2) its indurated character.

Mantoux tuberculin skin test (TST)

- The test is administered by injecting 0.1 ml of 5-TU PPD intradermally into the volar or dorsal surface of the forearm.
- Tests should be read between 48 and 72 h after injection,
- when the induration is maximum. Reading should be performed in a good light, with the forearm slightly flexed at the elbow. The basis of reading is the presence or absence of induration, which may be determined by inspection (from a side view against the light as well as by direct light) and by palpation.
- For standardization, the diameter of induration should be measured transversely to the long axis of the forearm and recorded in millimeters.

Induration measuring





Mantoux tuberculin skin test (TST)

FACTORS CAUSING FALSE-NEGATIVE TUBERCULIN SKIN TESTS

Factors related to the person being tested
- Infections
- Viral (measles, mumps, chicken pox, HIV)
- Bacterial (typhoid fever, brucellosis, typhus, leprosy, pertussis, overwhelming tuberculosis, tuberculous pleurisy)
- Fungal (South American blastomycosis)
- Live virus vaccinations (measles, mumps, polio, varicella)
- Metabolic derangements (chronic renal failure)
- Low protein states (severe protein depletion, afibrinogenemia)
- Diseases affecting lymphoid organs (Hodgkin's disease, lymphoma, chronic leukemia, sarcoidosis)
- Drugs (corticosteroids and many other immumosuppressive agents)
- Age (newborns, elderly patients with "waned" sensitivity)
- Stress (surgery, burns, mental illness, graft-versus-host reactions)

Factors related to the tuberculin used
- Improper storage (exposure to light and heat)
- Improper dilutions
- Chemical denaturation
- Contamination
- Adsorption (partially controlled by adding Tween 80)

Factors related to the method of administration
- Injection of too little antigen
- Subcutaneous injection
- Delayed administration after drawing into syringe
- Injection too close to other skin tests

Factors related to reading the test and recording results
- Inexperienced reader
- Conscious or unconscious bias
- Error in recording

GUIDELINES FOR DETERMINING A POSITIVE TUBERCULIN SKIN TEST REACTION

Induration ≥ 5 mm	Induration ≥ 10 mm	Induration ≥ 15 mm
HIV-positive persons	Recent arrivals (< 5 yr) from high-prevalence countries	Persons with no risk factors for TB
Recent contacts of TB case	Injection drug users	
	Residents and employees* of high-risk congregate settings: prisons and jails nursing homes and other health care facilities, residential facilities for AIDS patients, and homeless shelters	
	Mycobacteriology laboratory personnel	
Fibrotic changes on chest radiograph consistent with old TB	Persons with clinical conditions that make them high-risk: silicosis diabetes mellitus, chronic renal failure, some hematologic disorders (e.g., leukemias and lymphomas), other specific malignancies (e.g., carcinoma of the head or neck and lung), weight loss of > 10% of ideal body weight, gastrectomy, jejunoileal bypass	
Patients with organ transplants and other immunosuppressed patients (receiving the equivalent of > 15 mg/d Prednisone for > 1 mo)	Children < 4 yr of age or infants, children, and adolescents exposed to adults in high-risk categories	

* For persons who are otherwise at low risk and are tested at entry into employment, a reaction of > 15 mm induration is considered positive.

Interferon-gamma release assays (IGRAs)

- IGRAs detect the release of interferon-gamma (IFN-γ) from sensitised T cells in response to antigens, such as early secretory antigenic target (ESAT)-6 or culture filtrate protein (CFP)-10, which are encoded by genes specific to Mycobacterium tuberculosis and are not shared with BCG or opportunistic mycobacteria.
- IGRAs are more specific than skin testing and logistically more convenient, as they require a single blood test rather than two clinic visits.
- IGRA represents the first choice for individuals with HIV.

Other tests

- **ADA: Adenosine deaminase**

As adenosine aminohydrolase, or ADA) is an enzyme involved in purine metabolism. It is needed for the breakdown of adenosine from food and for the turnover of nucleic acids in tissues.

- **Stimulation of T cells by mycobacterial antigens leads to increased levels of adenosine deaminase in pleural, pericardial, cerebrospinal and ascitic fluid, and so may assist in confirming suspected TB**
- **Has high negative predictive value .Values of less than 35 ul in fluid makes TB diagnosis unlikly**
- **Evidence of caseating granuloma in histopathology may a clue for TB .**
- **Baseline blood tests:cbc,ESR,LFT,RFT**

Radiology

- Abnormalities seen on chest radiographs may be suggestive of, but are never diagnostic of, TB disease
- In some instances, a computerized tomography (CT) scan may provide additional information.
- In primary tuberculosis occurring as a is generally seen as a middle or lower lung zone infiltrate, often associated with ipsilateral hilar adenopathy. Atelectasis may result from compression of airways by enlarged lymph nodes. This manifestation is common in children.cavitations are rare in primary (in primary progressive)

Post-primary pulmonary TB

- Cavitation is common in this form of tuberculosis. The most frequent sites are the apical and posterior segments of the right upper lobe and the apical–posterior segment of the left upper lobe.
- Healing of the tuberculous lesions usually results in development of a scar with loss of lung parenchymal volume and, often, calcification
- As tuberculosis progresses, infected material may be spread via the airways into other parts of the lungs, causing a patchy bronchopneumonia
- Old, healed tuberculosis presents a different radiologic appearance from active tuberculosis. Dense pulmonary nodules, with or without visible calcification, may be seen in the hilar area or upper lobes.

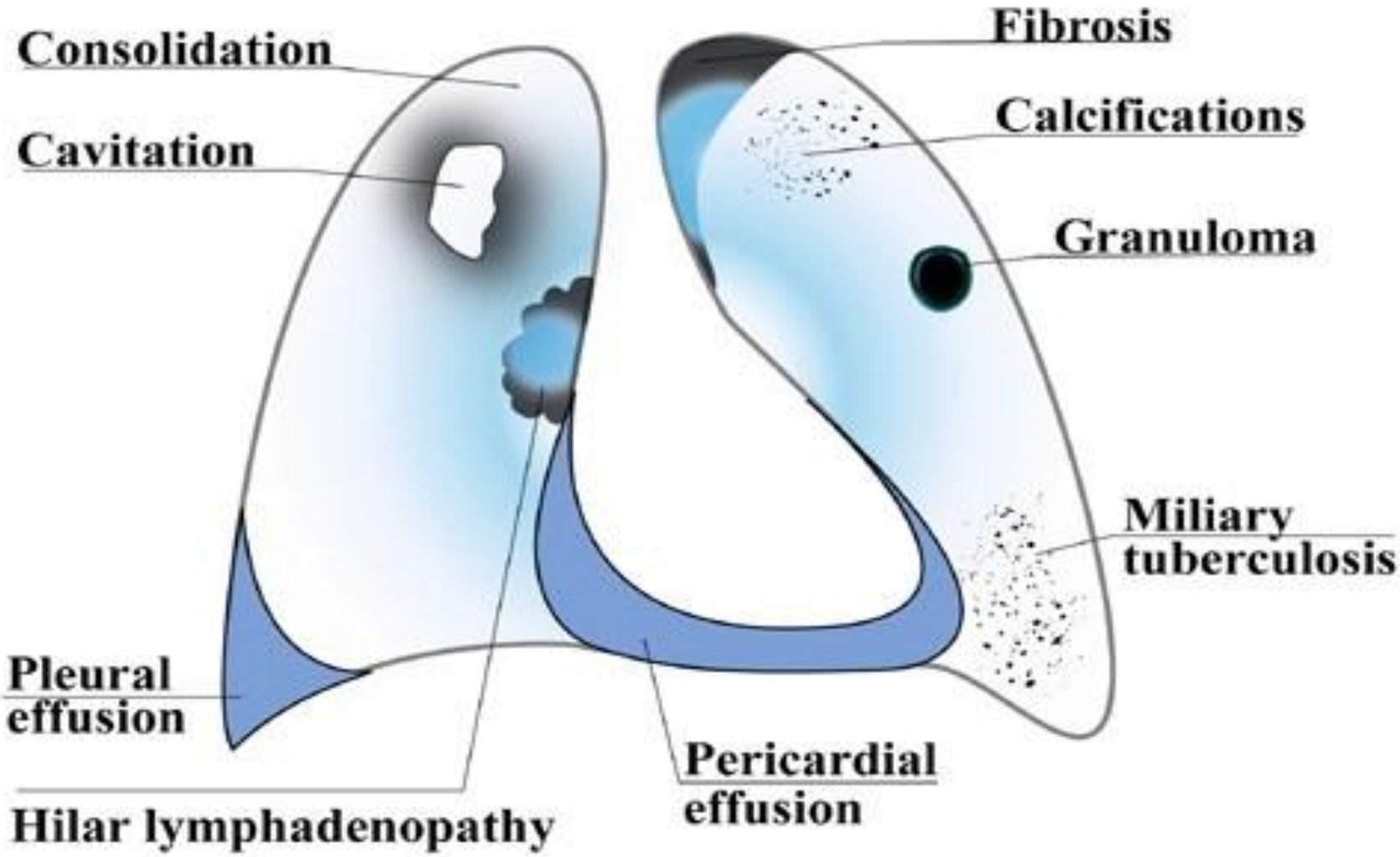
Post-primary pulmonary TB

- Smaller nodules, with or without fibrotic scars, are often seen in the upper lobes, tuberculosis. Pleural scarring may be caused by old tuberculosis
- upper-lobe volume loss often accompanies these scars. Nodules and fibrotic lesions of old
- healed tuberculosis have well-demarcated, sharp margins and are often described as “hard.”
- Bronchiectasis of the upper lobes is a nonspecific finding that sometimes occurs from previous pulmonary
- Pleural scarring may be caused by old tuberculosis
- Pericardial calcifications in 25% of TB pericarditis

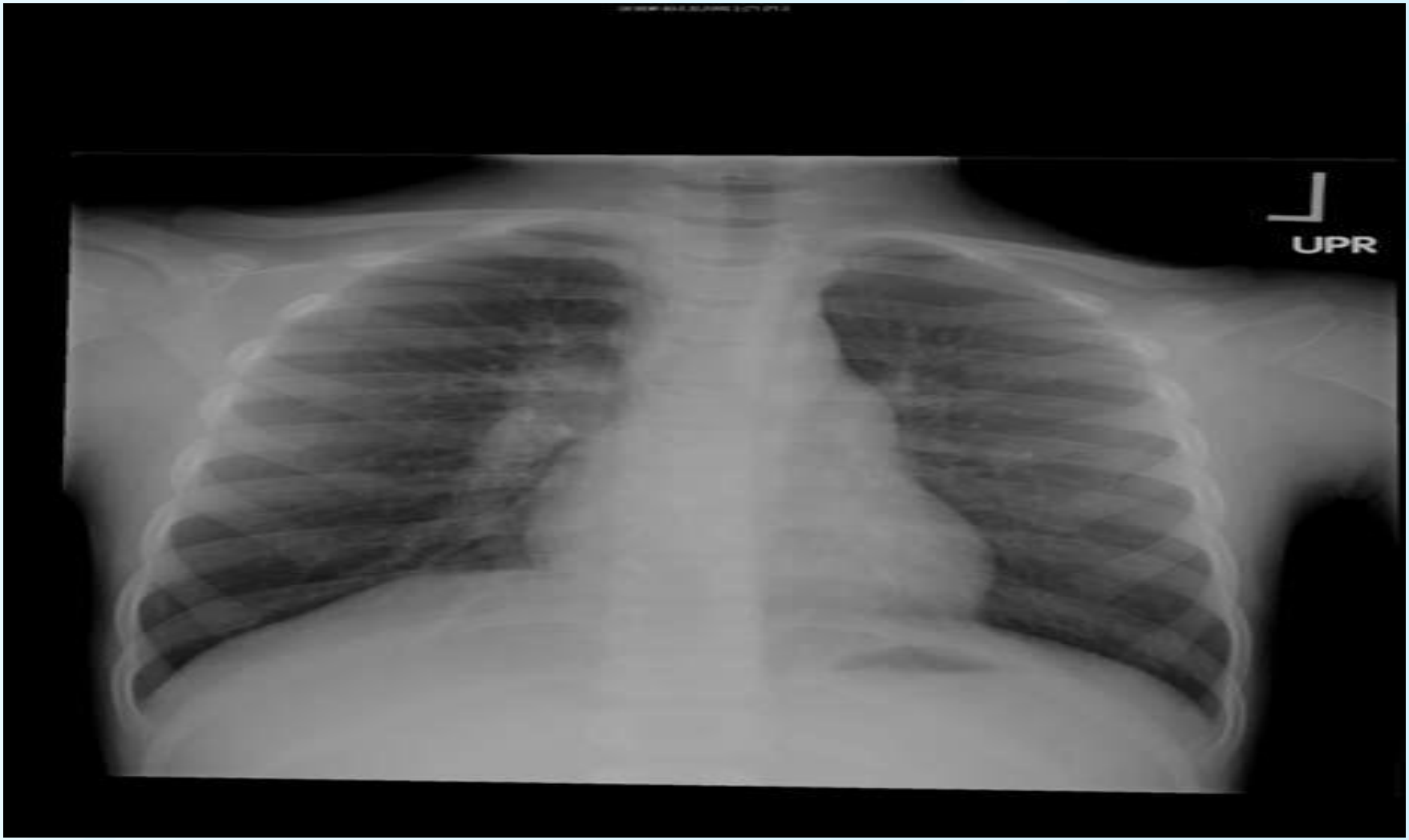
Radiology

- Others radiography according to site of involvement
- Echo (constrictive pattern)
- Spinal CT scan or MRI
- valuable in gauging the extent of disease, the amount of cord compression, and the site for needle biopsy or open exploration, if required, The major differential diagnosis is malignancy, which tends to affect the vertebral body and leave the disc intact.
- GIT
  - Ultrasound or CT may reveal thickened bowel wall, abdominal lymphadenopathy, mesenteric thickening or ascites. Barium enema and small bowel enema reveal narrowing, shortening anddistortion of the bowel, with caecal involvement predominating.

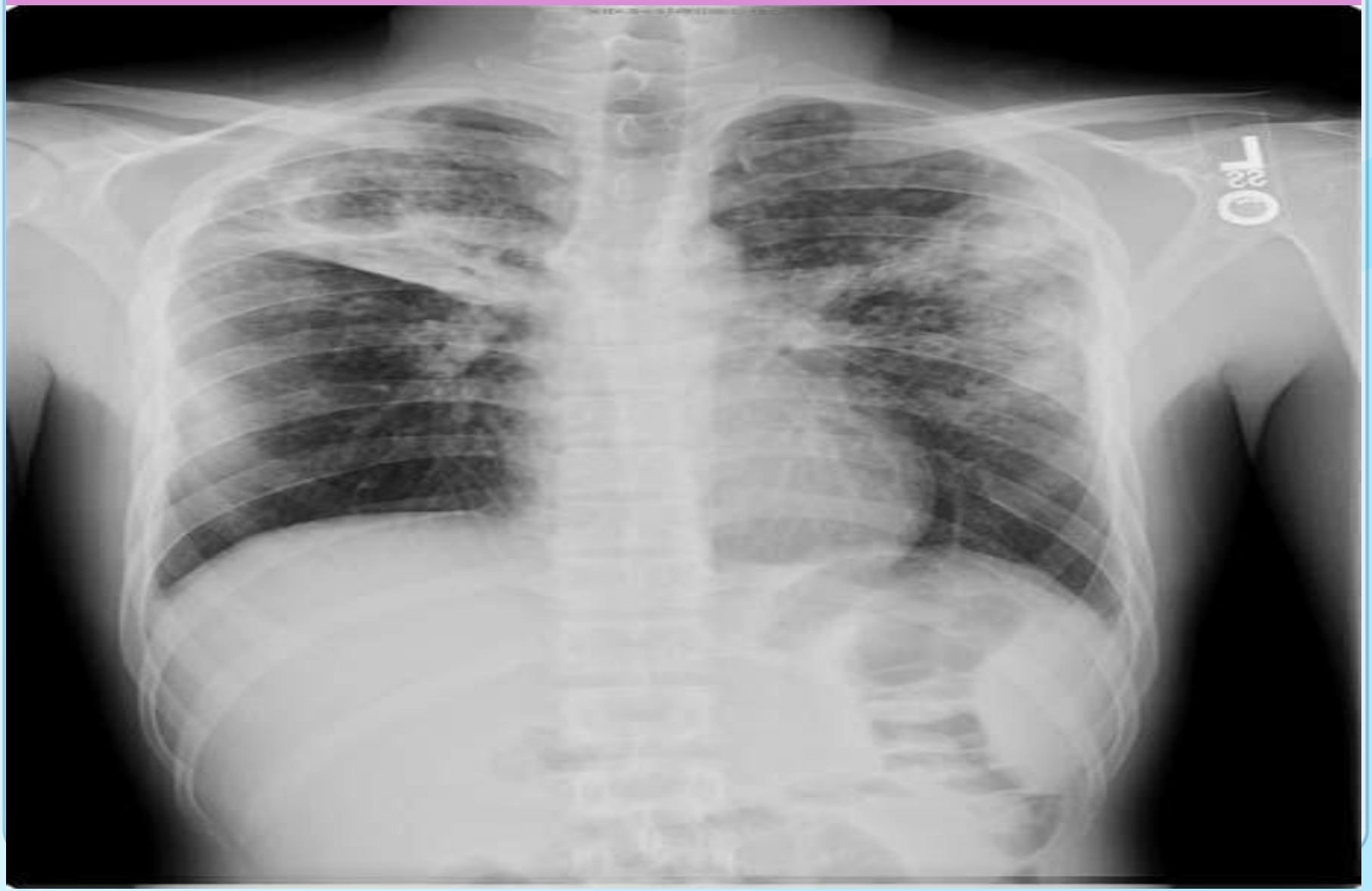
Manifestations of tuberculosis



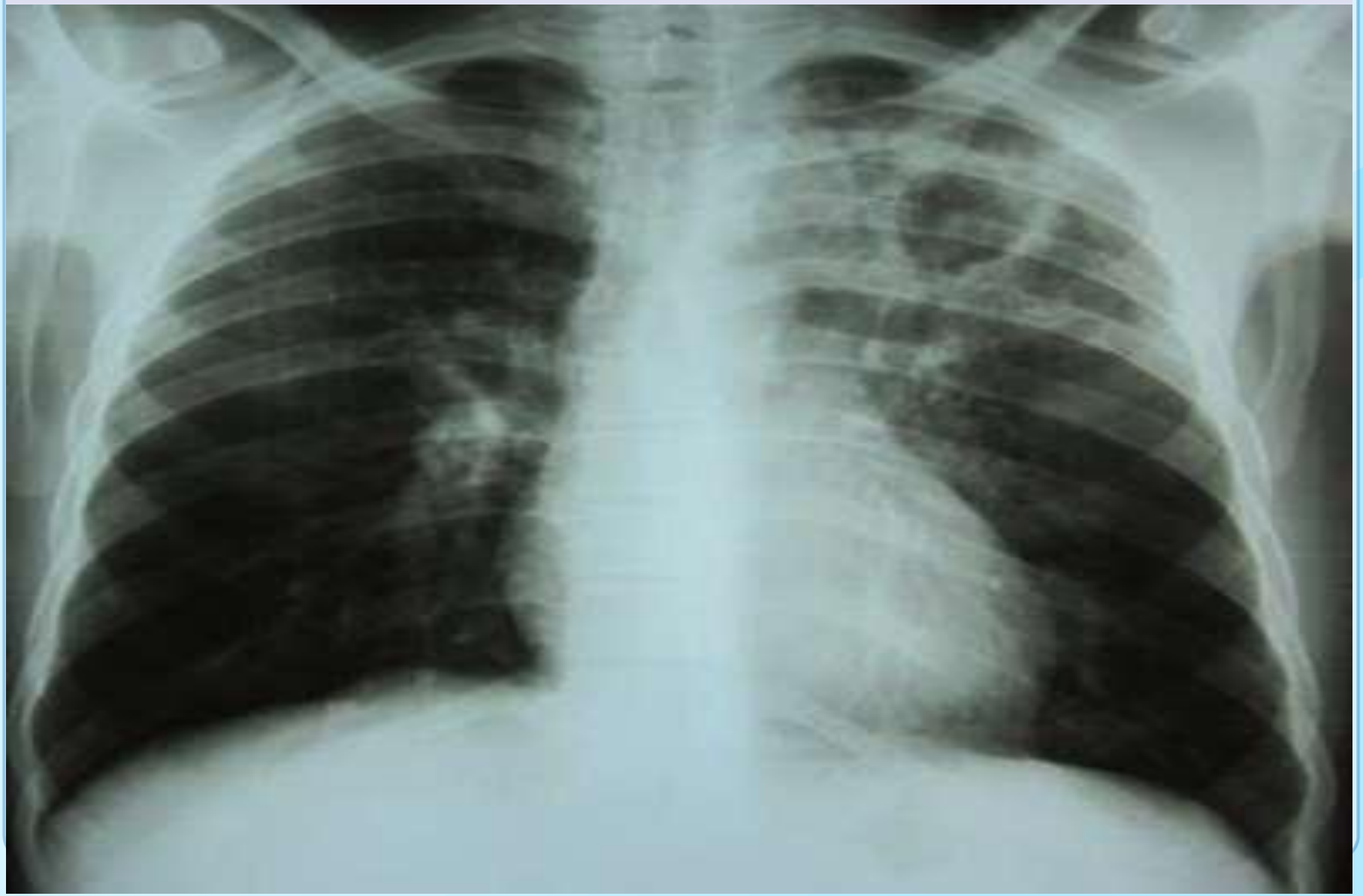
Primary TB



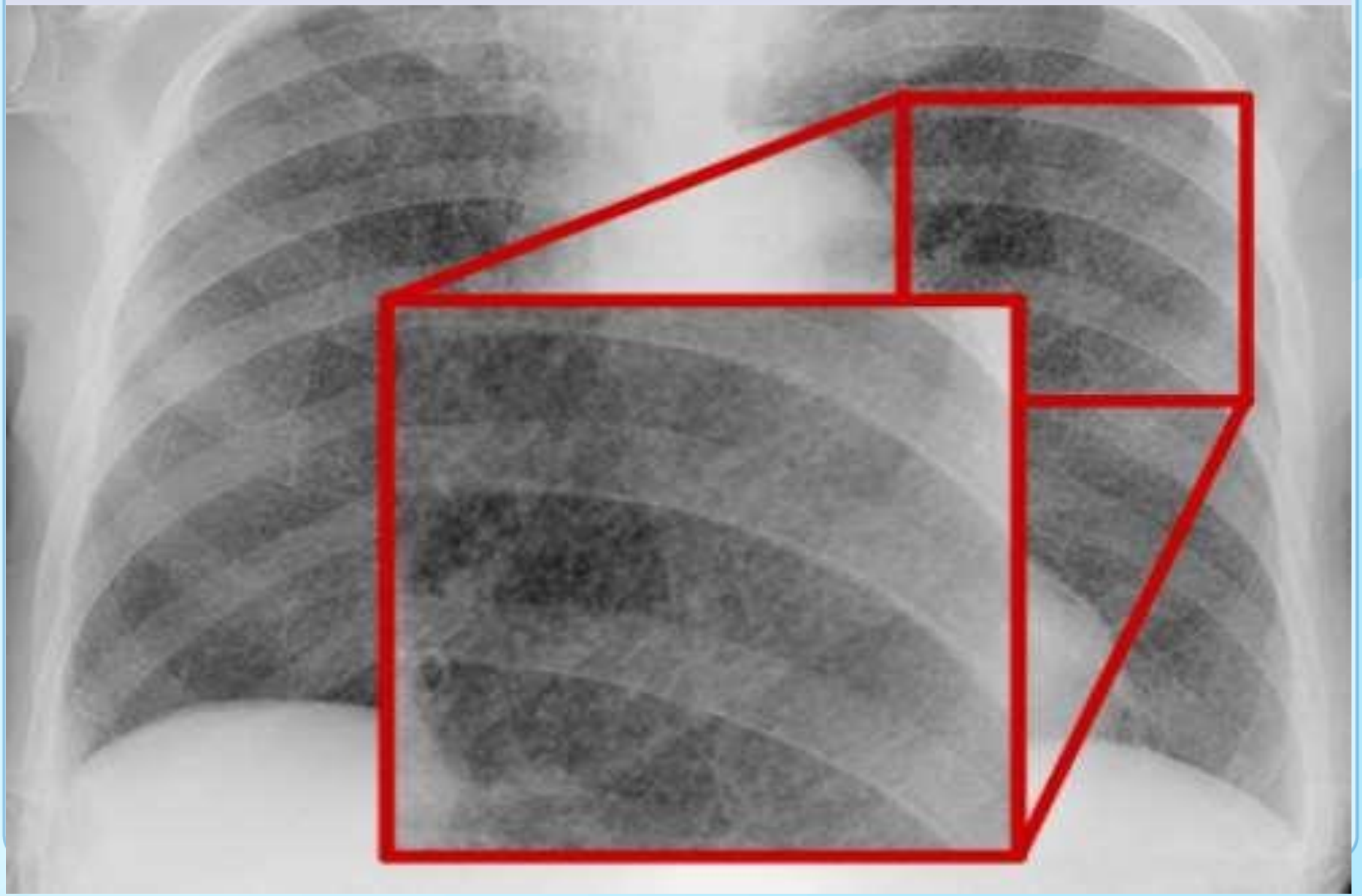
Post-primary: Pulmonary TB



Post-primary:
Pulmonary TB



Military TB



Diagnostic process

- Epidemiologic or medical risk factors

  "Membership in a risk group"

  - Foreign-born from high prevalence areas
  - Substance abuse, homelessness, correctional facilities, institutional residence
  - HIV and other immunosuppression (e.g., TNFalpha inhibitors)
  - CXR suggestive of prior TB (apical fibrosis)

- Clinical presentation

  • symptoms suggestive of TB?

  • Imaging suggestive of TB?

Yes? Obtain appropriate specimens for AFB smear and culture (Lab confirmation)

Treatment

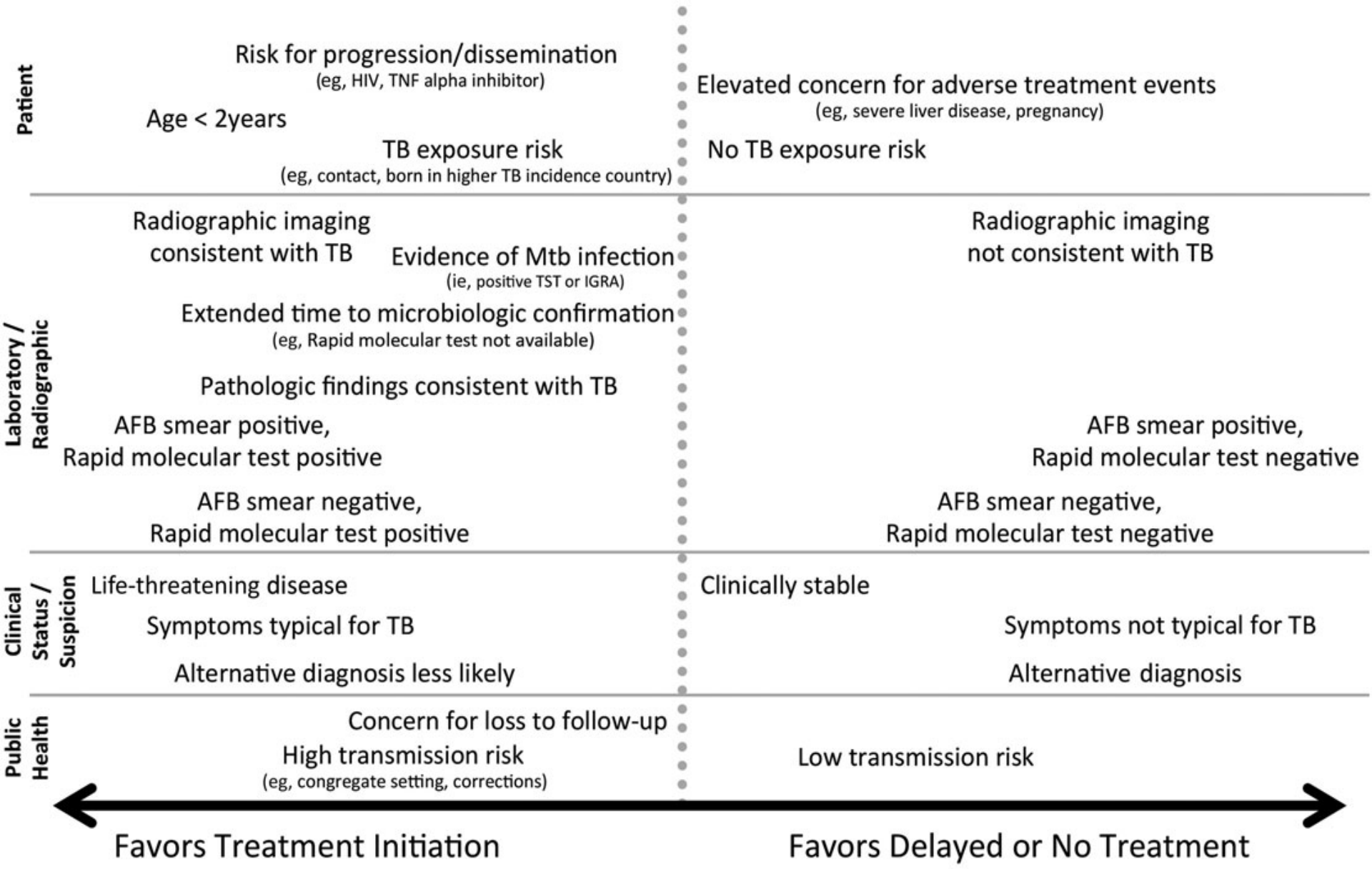
Aims of TB Treatment

- Cure the patient of TB
- Prevent death from active TB or its latent effects
- Prevent relapse of TB
- Decrease transmission of TB to others
- Prevent the development of acquired resistance
- Provide safest, most effective therapy in shortest time
- Ensure adherence and completion of therapy

Develop Treatment and Monitoring Plan

- Plan should include
- Description of treatment regimen
- Methods for assessing/ensuring adherence
- Monitoring methods for treatment response and adverse events

Deciding to Initiate Treatment



Basic Principles of TB treatment

- Appropriate combination of drugs to kill different bacterial population
- Drugs are given for the required duration to kill the bacilli
- Drugs are given in the correct dosage to achieve the therapeutic effect

Case Definitions

Case classification	Definition
Pulmonary smear-positive TB (PTB+)	• A patient with at least one sputum specimen positive for AFB, including any scanty smear result.
Pulmonary smear negative TB (PTB-) but positive on Xpert (MTB+/RIF)	(If Xpert is available) • A patient with symptoms suggestive of TB with two sputum specimens negative for AFB; and • Found positive on Xpert MTB+/RIF- (MTB detected Rifampicin Susceptible)
Pulmonary smear-negative (PTB-)	A. (If X-ray is available) • A patient with symptoms suggestive of TB with two sputum specimens negative for AFB; and • Xpert MTB/RIF (if available) is Negative and • Chest X-ray abnormalities consistent with active TB; and • Diagnosis is made by a qualified physician
Extra-pulmonary TB (EPTB)	• A patient with TB of organs other than the lungs as confirmed by a qualified physician e.g pleura, lymph nodes, abdomen, genitourinary tract, skin, joits and bones, meninges.

Case classification	Definition
New	• A patient who has never received anti-TB drugs; or • A patient who received anti-TB drugs for less than one month
Relapse	• Relapse patients have previously been treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection).
Treatment after failure	• Treatment after failure patients are those who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment.
Treatment after loss to follow up/default	• Treatment after loss to follow-up patients have previously been treated for TB and were declared lost to follow-up at the end of their most recent course of treatment. (These were previously known as treatment after default patients.)
Transfer in	• A patient already registered for treatment in a DOTS centre and who is subsequently transferred to another registration unit
Other (s)	• Other previously treated patients are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

Current Anti-TB Drugs

- Four first-line drugs considered standard treatment:
- Isoniazid (INH)
- Rifampin (RIF)
- Pyrazinamide (PZA)
- Ethambutol (EMB)
- Rifabutin and rifapentine

Second-line drugs

- Amoniglycosides – injectable : streptomycin ,kanamycin, Amikacin, Capromycin
- Thiomides – Ethionamide, Prothionamide.
- Cycloserine.
- Para amino salicylic acid (PASA)
- Levofloxacin ,moxifloxacin

New Anti TB drugs

- **Bedaquiline**
- Delamanid
- Pretomanid
- NC-002, NC-003
- Sutezolid
- SQ 109
- Benzothiazinones

Repurposed Anti TB drugs

- Linezolid
- Clofazamine
- Imipenem/ Meropenem
- Amoxicillin – Clavulanate
- Thioacetazone
- Clarithromycin

TB Disease Treatment Regimens

Table 3 : Standardized treatment regimen for each diagnostic category (Adults)

TB diagnostic category	Type of Patient	Treatment regimen	
		Intensive phase (Daily)	Continuation phase (Daily)
Cat. I	• New smear-positive bacteriologically positive PTB patients • New smear-negative PTB • New Extra-pulmonary TB • New concomitant/ associated HIV/AIDS	2(HRZE)	4 (HR)
Cat. II	• Sputum smear-positive PTB with history of treatment of one month or more • Relapse • Treatment failure after Cat. I Treatment • after loss to follow up • Others	2(HRZE)S/ 1(HRZE)	5 (HRE)

TABLE 55.2 Categorywise treatment regimens for tuberculosis (adopted from WHO guidelines 2010)*

Category	*Intensive phase*	*Continuation phase*	*Duration (months)*	*Comment*
I New patient	2[$] HRZE daily	4[$] HR daily	6[$]	Optimal
	2 HRZE daily	4 HR thrice weekly	6	Acceptable if DOT ensured
	2 HRZE thrice weekly	4 HR thrice weekly	6	Acceptable if DOT ensured, and no HIV coinfection or its risk
II Previously treated patients pending DST result	2 HRZES daily + 1 HRZE daily	5 HRE daily	8	For patient with low/medium risk of MDR-TB (failure, default, etc.)
	Empirical[£] (standardized) MDR-regimen	Empirical (standardized) MDR-regimen	18–24 or till DST result	For patient with high risk of MDR-TB (failure, 2nd default, contact of MDR-TB, etc.)

TB Disease Treatment Regimens

- Four regimens recommended for treatment of drug-susceptible TB, with different options for number of doses and for length of continuation phase
- Initial phase: standard four drugs (INH, RIF, PZA, EMB) for 2 months (one excludes PZA)
- Continuation phase: additional 4 months; 7 months for some patients

Drug Regimens for Microbiologically Confirmed Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms

	Intensive Phase		Continuation Phase				
Regimen	Drug[a]	Interval and Dose[b] (Minimum Duration)	Drugs	Interval and Dose[b,c] (Minimum Duration)	Range of Total Doses	Comments[c,d]	Regimen Effectiveness
1	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182–130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis.	Greater
2	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	110–94	Preferred alternative regimen in situations in which more frequent DOT during continuation phase is difficult to achieve.	
3	INH RIF PZA EMB	3 times weekly for 24 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	78	Use regimen with caution in patients with HIV and/or cavitary disease. Missed doses can lead to treatment failure, relapse, and acquired drug resistance.	
4	INH RIF PZA EMB	7 d/wk for 14 doses then twice weekly for 12 doses[e]	INH RIF	Twice weekly for 36 doses (18 wk)	62	Do not use twice-weekly regimens in HIV-infected patients or patients with smear-positive and/or cavitary disease. If doses are missed, then therapy is equivalent to once weekly, which is inferior.	Lesser

TB Disease Treatment Regimens

- When to use 7-month continuation phase:
- Disease is cavitary and sputum culture is positive at end of initial phase;
- Initial phase excluded PZA; or
- Once-weekly INH and RPT used in continuation phase, and culture is positive at end of initial phase

Extrapulmonary TB

- In most cases, treat with same regimens used for pulmonary TB.
- Bone and Joint TB, or TB Meningitis ,Treatment extended > 6 months depending on site of disease
- 12 months of therapy is recommended for meningeal TB, including involvement of the spinal cord in cases of spinal TB
- In TB meningitis Streptomycin replaces Ethambutol

Directly Observed Therapy (DOT)

- Health-care worker watches patient swallow each dose
- DOT is preferred management strategy for all patients
- Can reduce acquired drug resistance, treatment failure, and relapse
- Nearly all regimens can be intermittent if given as DOT
- DOT reduces total number of doses and encounters
- For drug-resistant TB, use daily regimen and DOT

TREATMENT REGIMENS FOR SPECIFIC SITUATIONS

Pregnant Women

- Initial regimen should consist of INH, RIF, and EMB
- SM is contraindicated; PZA not contraindicated, but detailed data on teratogenicity not available
- If PZA not used, duration of therapy is 9 months
- If treating MDR TB in pregnancy, consult MDR TB expert
- Breast-feeding not contraindicated for women being treated for TB disease
- Vitamin B6 supplementation recommended if taking INH

Infants and Children

- Treat with same regimens recommended for adults, with exception that EMB not used routinely in children
- Treat as soon as diagnosis suspected
- For disseminated TB or TB meningitis in children, treat for 9–12 months

chronic liver disease

- **ATT in patients with chronic liver disease should be used cautiously and the choice of regimen should be based on severity of underlying liver disease.**

Child-Turcotte-Pugh score	Liver disease	Treatment
≤7	Stable	Recommend treatment with two potentially hepatotoxic drugs, likely to be well tolerated; avoid pyrazinamide
8–10	Advanced	Recommend a regimen with only one potentially hepatotoxic drug; rifampicin is preferred over isoniazid; pyrazinamide should not be used
≥11	Very advanced	Recommend treatment regimen with no potentially hepatotoxic drugs; can use (streptomycin, ethambutol, fluoroquinolones, amikacin, kanamycin) and other second-line oral drugs for 18–24 months.

HIV-Infected Persons

- Management of HIV-related TB is complex
- Should be provided in consultation with experts in treatment of both HIV and TB
- Can be treated with standard regimens except:
- Do not use once-weekly continuation-phase INH and RPT
- In patients with advanced HIV, use daily or 3x weekly therapy

(cont.)

- If possible, use a rifamycin for the entire course of therapy, along with ART
- A major concern: RIF interacts with some PIs and NNRTIs
- Rifabutin has fewer drug interactions and may be used instead of RIF
- Drug dosages may need adjusting; consult expert

Renal insufficiency/end-stage renal disease

- Some TB drugs are cleared by the kidneys; thus the dosing must be altered with renal disease
- Rather than decrease dosage size, increase dosing interval
- Ethambutol and streptomycin should be used with caution in renal impairment, with appropriate dosing interval monitoring of drug levels.

Drug Resistant Tuberculosis

Drug-resistant tuberculosis is confirmed through laboratory tests that demonstrate growth of infecting isolates of Mycobacterium tuberculosis in-vitro in the presence of one or more anti-tuberculosis drugs. By definition, there are four different categories of drug resistance, namely:

- Mono-resistance: resistance to one anti-TB drug.
- Poly-resistance: resistance to more than one anti-TB drug, other than isoniazid and rifampicin.
- Multidrug-resistance (MDR): resistance to at least isoniazid and rifampicin, the two most potent anti-TB agents.
- Extensive drug-resistance (XDR): MDR TB, plus resistance to at least one of the fluoroquinolones, and at least one of three injectable second-line drugs (capreomycin, kanamycin and amikacin).

Management Of MDR TB

- Presents difficult treatment problems
- Lengthy, multi-drug regimen
- Side effects common
- Management complex

- Treatment must be individualized

- Clinicians unfamiliar with treatment of MDR TB should seek expert consultation

- Always use DOT to ensure adherence

Management Of MDR TB

- 6 months intensive treatment (always including an injectable drug) followed by at least an 18 month continuation phase(longer regimen)
- All oral longer regimens are now used
- Shorter all oral bedaquiline containing regimen 9-12 months
- Recently ,the 6- month bedaquline,pretomanid,linozolid and moxifloxacin (BPaLM regimen)is approved for special conditions .

- Only specialist physicians at the referral hospitals can initiate MDR treatment

MDR TB TREATMENT

- Use pyrazinamide and any first-line oral agents that may be effective.
- Use an injectable agent to which the strain is susceptible, and consider an extended duration of use (12 months or possibly the whole treatment period). If the strain is resistant to all injectable agents, use of one that the patient has not previously received is recommended.
- Use a later-generation fluoroquinolone, such as moxifloxacin, high-dose levofloxacin, or possibly gatifloxacin.
- Use all second-line oral bacteriostatic agents have not been used extensively in a previous regimen or any such agents that are Likely to be effective.
- (

MDR TB TREATMENT

- Add bedaquiline or delamanid and one or more of the following drugsc: clofazimine, linezolid, amoxicillin/clavulanic acid, clarithromycin, and carbapenems such as imipenem/cilastatin and meropenem.
- The simultaneous use of bedaquiline and delamanid is not recommended
- Consider treatment with high-dose isoniazid if low-level resistance to this drug is documented.
- Consider adjuvant surgery if there is localized disease.
- Enforce strong infection-control measures

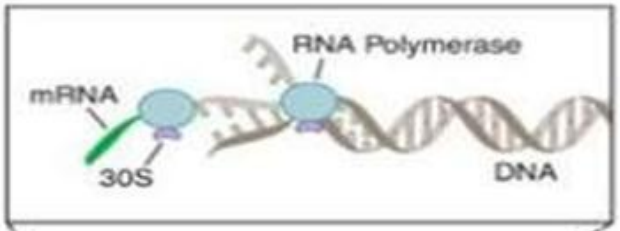
Treatment Interruptions

- Treatment interruption is common
- Restart or continue therapy based on when interruption occurred and duration of interruption
- Treatment Interruption During Initial Phase
- If lapse ≥14 days, restart treatment
- If lapse <14 days, continue treatment to completion as long as all doses completed within 3 months

Treatment Interruption During Continuation Phase

- If patient received ≥80% of doses and
  - Sputum smear was negative on initial testing, further therapy may not be needed
  - Sputum smear was positive on initial test, continue therapy
- If patient received <80% of doses, and lapse is
  - <3 months long, continue therapy
  - >3 months long, restart therapy from beginning of initial phase

Anti TB Drugs pharmacology



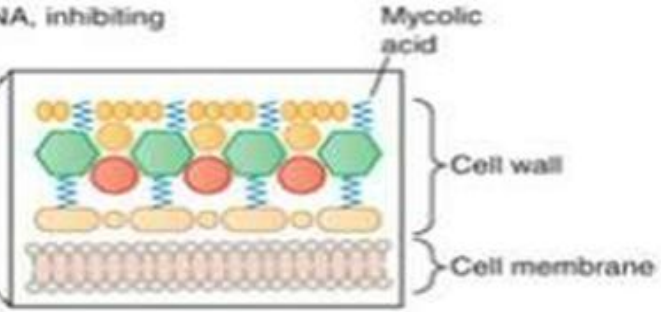
Approved Drugs

Fluoroquinolone:
inhibits DNA synthesis and supercoiling by targeting topoisomerase

Rifamycin:
inhibits RNA synthesis by targeting RNA polymerase

Streptomycin:
inhibits protein synthesis by targeting the 30S ribosomal subunit

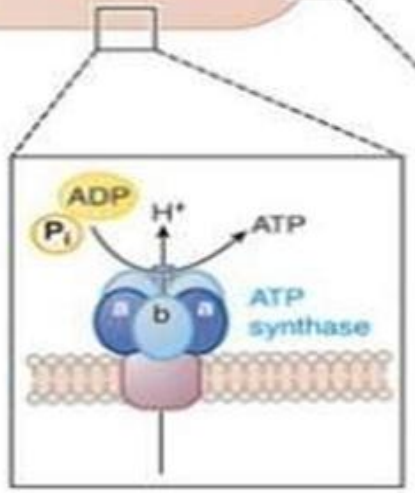
Macrolides:
target 23S ribosomal RNA, inhibiting peptidyl transferase



Isoniazid and Ethionamide:
inhibit mycolic acid synthesis

Ethambutol:
inhibits cell wall synthesis

Pyrazinamide:
inhibits cell membrane synthesis



Experimental Drugs

TMC-207 (R207910, TMC):
inhibits ATP synthase

PA-824:
inhibits mycolic acid and protein biosynthesis; possibly acts via generation of toxic radicals

	Isoniazid	Rifampicin	Pyrazinamide	Streptomycin	Ethambutol
Mode of action	Cell wall synthesis	DNA transcription	Unknown	Protein synthesis	Cell wall synthesis
Major adverse reactions	Peripheral neuropathy[1] Hepatitis[2] Rash	Febrile reactions Hepatitis Rash Gastrointestinal disturbance	Hepatitis Gastrointestinal disturbance Hyperuricaemia	8th nerve damage Rash	Retrobulbar neuritis[3] Arthralgia
Less common adverse reactions	Lupoid reactions Seizures Psychoses	Interstitial nephritis Thrombocytopenia Haemolytic anaemia	Rash Photosensitisation Gout	Nephrotoxicity Agranulocytosis	Peripheral neuropathy Rash

[1]The risk may be reduced by prescribing pyridoxine. [2]More common in patients with a slow acetylator status and in alcoholics. [3]Reduced visual acuity and colour vision may be reported with higher doses and are usually reversible.

Site of care

- Most patients can be treated at home.
- Admission
- Admission to a hospital unit with appropriate isolation facilities should be considered in :
- where there is uncertainty about the diagnosis,
- intolerance of medication,
- questionable treatment adherence,
- adverse social conditions
- or a significant risk of multidrug-resistant TB (culturepositive after 2 months on treatment, or contact with known multidrug-resistant TB)
- Severly ill pt

Patient Monitoring

Recommended Examinations for Baseline Monitoring

Patient	Recommended Test
All patients	Measure aminotransferases (i.e., AST, ALT), bilirubin, alkaline phosphatase, and serum creatinine and a platelet count
Patients at risk for hepatitis B or C (e.g., injection drug user, born in Asia or , or HIV infected)	Conduct serologic tests
Patients who are taking EMB	Test visual acuity (Snellen chart) and color vision (Ishihara)
HIV-infected patients	Obtain CD4+ lymphocyte count

Patient Monitoring (cont.)
Monitoring During Treatment

Patient	Recommendations
All patients	Repeat at least monthly clinical evaluations to • Identify possible adverse reactions to medications • Assess adherence
Patients who are taking EMB	• Question monthly regarding visual disturbances • Repeat monthly testing for visual acuity (Snellen chart) and color vision (Ishihara) for patients whose dose exceeds 15-20 mg/kg and those who have been receiving EMB for >2 months
Patients who have extrapulmonary TB disease	Evaluation depends on • Sites involved • Ease with which specimens can be obtained

Evaluating Response to Treatment

- **Assess patient's response to treatment using three methods:**
  - Clinical evaluation, bacteriological examination, chest radiograph
- **Conduct clinical evaluations at least monthly; after 2 months of therapy, if symptoms do not resolve, reevaluate for**
  - Potential drug-resistant disease
  - Nonadherence to drug regimen

Evaluating Response to Treatment (cont.)

- **Bacteriological examination**

If cultures do not convert to negative after 3 months of therapy, evaluate patient for drug resistance or adherence issues; after 4 months, consider treatment failed

- **Chest radiograph**

Patients with initially negative cultures should have chest radiograph after 2 months of treatment and at completion of therapy

Evaluating Response to Treatment (cont.)

- **Monitor for adverse reactions**
- **Common adverse reactions include**
  - Gastrointestinal problems
  - Hepatitis
  - Rash
  - Fever

Hepatotoxicity during treatment

- If serum transaminase concentrations are more than five
- times the ULN (with or without symptoms) or more than three times the ULN with jaundice and/or hepatitis symptoms, then potentially hepatotoxic medications should be stopped immediately and the patient evaluated promptly.
- Serologic tests for hepatitis A, B, and C viruses should be obtained, and the patient should be evaluated for biliary disease, use of alcohol, and other hepatotoxic drugs.
- Some experts recommend interrupting treatment for lesser increases in patients with cirrhosis or encephalopathy.

Hepatotoxicity during treatment

- After ALT returns to less than two times the ULN, rifampin may be restarted with or without ethambutol.
- After 3 to 7 days, isoniazid may be reintroduced, subsequently
- rechecking ALT.
- If symptoms recur or ALT increases, the last drug added should be stopped.
- For those who have experienced prolonged or severe hepatotoxicity,
- but tolerate reintroduction with rifampin and isoniazid, rechallenge with pyrazinamide may be hazardous.
- In this circumstance, pyrazinamide may be permanently
- discontinued, with treatment extended to 9 months

Other treatment

- **Glucocorticoids**
- **Indications**
- **Strong recommendation**
- **pericardial**
- **meningeal disease**
- **Other indications**
- **Seriously ill patients to buy time for chemotherapy to become effective.**
- **To control drug hypersensitivity reaction**
- **Adrenal TB**
- **in children with endobronchial disease. They may confer benefit in TB of the ureter, pleural effusions and extensive pulmonary disease**

Surgery

- Surgery should be considered in
- cases complicated by :
- massive haemoptysis,
- loculated empyema,
- constrictive pericarditis,
- lymph node suppuration,
- and spinal disease with cord compression,
- but usually only after a full course of antituberculosis treatment.

Treatment for Latent TB Infection (LTBI)

- 5%-10% will develop TB disease if untreated
- Treatment of LTBI essential to controlling and eliminating TB disease
- Reduces risk of LTBI to TB disease progression
- Use targeted testing to find persons at high risk for TB who would benefit from LTBI treatment
- Several treatment regimens available

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- Several treatment regimens available
  - Isoniazid alone alone 6 months
  - Isoniazid with rifampicin 3 months daily
  - Rifampicin daily4 months
  - 3 months of once weekly isoniazid and rifapentine

Candidates for Treatment of LTBI

- High-risk persons with positive IGRA test or TST reaction of ≥5 mm
- High-risk persons with positive IGRA test or TST reaction of ≥10 mm
- Low-risk persons with positive IGRA test or TST reaction of ≥15 mm
- Some contacts should be evaluated and treated for LTBI even with negative TB test results:
- Young children <5 years of age
- Immunosuppressed persons
- Others at risk for rapid progression to TB disease once infected
- Always rule out TB disease with chest radiograph and medical evaluation before treating for LTBI

BCG Vaccination

- BCG (the Calmette–Guérin bacillus), a live attenuated vaccine derived from M. bovis, is the most established TB vaccine.
- It is administered by intradermal injection and is highly immunogenic.
- BCG appears to be effective in preventing disseminated disease, including tuberculous meningitis, in children, but its efficacy in adults is inconsistent and new vaccines are urgently needed.
- Current vaccination policies vary worldwide according to incidence and health-care resources, but usually target children and other high-risk individuals

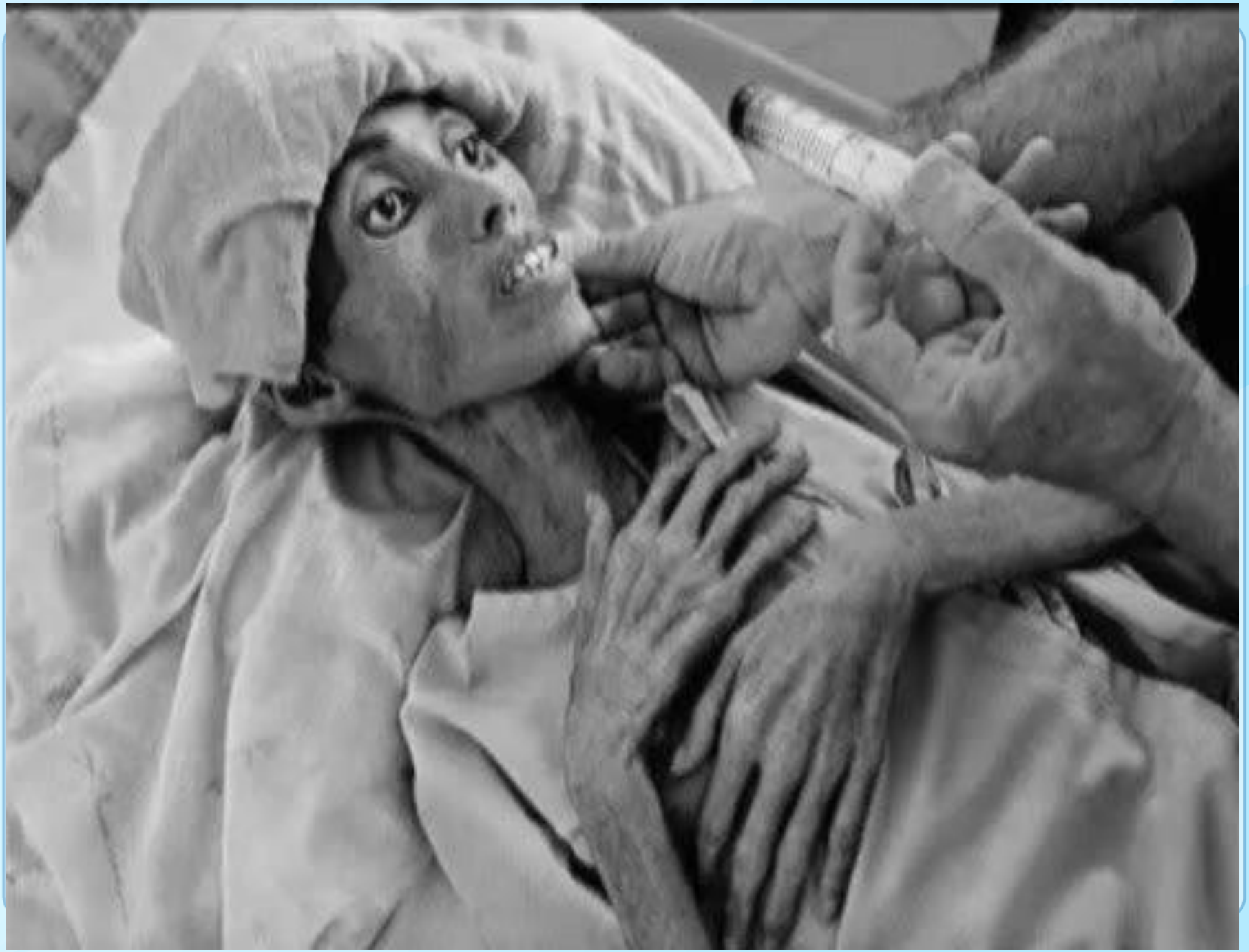
New Vaccination

- Recently ,an investigational TB vaccine ,M72/AS01E was found to be significantly effective in phase 11 b trial .
- It prevent progression of latent TB

Prognosis

- If treated ,85-95% will be cured
- 5% risk of relapse
- If untreated:
- 60% will die
- 20% chronic

If TB Is Not Adequately and Effectively Treated, Then This Will Happen




IT'S
TIME!
END
TB

WORLD TB DAY

MARCH 24

WHO's End TB Strategy

- The strategy aims to end the global TB epidemic, with targets to reduce TB deaths by 95% and to cut new cases by 90% between 2015 and 2035, and to ensure that no family 100% is burdened with catastrophic expenses due to TB.

Thank you